

INFLUENCE OF DIET IN ALZHEIMER'S DISEASE: THE ROLE OF CARBOHYDRATE
INTAKE AND KETOGENIC THERAPY

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Abstract

Background: One in every 9 persons age 65 years and older and 1 in every 3 persons age 85 years and older has Alzheimer's disease. The etiology of the disease is not well understood. For decades, cerebral accumulation of amyloid proteins and tau neurofibrillary tangles has been thought to be the culprit. While amyloid and tau are still risk factors, mounting evidence is shifting the framing of Alzheimer's to a disease of disordered metabolism. Individuals with Alzheimer's consistently exhibit decreased cerebral metabolism due to impaired glucose utilization. Those with chronic hyperglycemia present with greater accumulation of cerebral amyloid plaques and more severe reductions in brain metabolism increasing Alzheimer's risk. Little data exist exploring the role of dietary intake, namely carbohydrate intake and glycemic load, in amyloid processing or altering brain bioenergetics through manipulation of dietary macronutrient intake.

Methods: Two studies were conducted to assess the questions proposed in this dissertation. First, we performed cross-sectional analyses of dietary glycemic measures (high glycemic load diet pattern [HGLDiet], sugar intake, carbohydrate intake and glycemic load) with cerebral amyloid burden (measured by florbetapir F-18 PET) and cognitive performance in 128 cognitively normal older adults participating in the University of Kansas Alzheimer's Prevention Program. Second, we recruited 15 participants with a diagnosis of Alzheimer's disease to a single-arm clinical trial of a medium chain triglyceride supplemented ketogenic diet (MCT-KD) for 3 months to assess feasibility and obtain preliminary efficacy data. At month 3, participants terminated the MCT-KD and resumed a normal diet for a 1-month washout period.

Ketone generation was monitored through daily checking of urinary ketone status by the participant and monthly serum β -hydroxybutyrate assessment. Dietary intake was collected through monthly 3-day food records. Cognition was measured through administration of the Mini-Mental State Exam and the Alzheimer's Disease Assessment Scale-cognitive subscale at baseline, after 3 months of the dietary intervention and following a 1-month discontinuation of the MCT-KD.

Results: In the observational study, individuals with elevated amyloid had greater consumption of the HGLDiet pattern ($p=0.015$). The HGLDiet pattern was positively associated with amyloid burden both globally and in all regions of interest independent of age, gender, and BMI (all p -values ≤ 0.001). Individual dietary glycemic measures (sugar intake, carbohydrate intake and glycemic load) were also positively associated with global amyloid load and nearly all regions of interest independent of age, gender and BMI (p -values ≤ 0.05). Higher sugar consumption was associated with poorer global cognitive performance (Global Composite and Mini-Mental State Exam) and performance on subtests of Digit Symbol, Trailmaking B, and Block Design when controlled for age, gender, and education. In the clinical trial, the MCT-KD was feasible in individuals with AD as 10 of the 15 participants produced urinary and serum ketones during the 3-month intervention. Urinary acetoacetate was detected an average of 54.5 (60.6%) days of the intervention in study completers. Serum β -hydroxybutyrate was significantly elevated above baseline at all 3 monthly time points during the diet intervention ($p\leq 0.001$ for each). Improvements in ADAS-cog scores were observed from baseline to month 3 (4.1 point mean improvement, $p=0.02$) and improvements diminished after the 1-month washout.

Conclusion: A dietary pattern high in carbohydrate, especially highly glycemic carbohydrates, was associated with biomarkers for AD risk. A ketogenic diet restricted in carbohydrate and higher in fat may elicit cognitive benefit in individuals already diagnosed with AD.

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Chapter One: Introduction

Alzheimer's Disease

In the US, Alzheimer's disease (AD) is the most common form of dementia and affects an estimated 5.4 million Americans or 1 of every 9 people over the age of 65. AD accounts for 60 to 80 percent of the total cases of dementia (1). Apart from the personal burden of AD, this disease also drastically affects the nation economically costing an estimated \$457 billion in 2016 (1). Future predictions of the effect of AD are also quite staggering. If no progress is made in altering the course of AD onset and progression, it is estimated that nearly 14 million people will have AD by 2050 with a cost of over \$1 trillion each year (2). Furthermore, the toll of AD is magnified when physical and emotional burden placed on caregivers and family members is considered (3, 4).

AD is a progressive neurodegenerative disease that is not a normal aspect of aging, although the greatest risk factor for the development of AD is age (1). It is characterized by formation of plaque lesions from abnormal cerebral accumulation of amyloid-beta ($A\beta$) proteins, accumulation of neurofibrillary tau protein tangles and progressive brain atrophy resulting in significant reduction in brain volume (5). Symptoms include progressive cognition and memory impairment, changes in behavior, depression and decline in ability to carry out daily activities (5, 6).

The etiology of Alzheimer's disease is not well understood (7). Evidence suggests that a myriad of determinants could likely contribute to AD pathology. Several hypotheses have been proposed in an attempt to explain the cause of AD onset.

AD as a Metabolic Disease

The long-standing theory of AD etiology posits that abnormal A β accumulation in the brain drives the progression of AD (8). Individuals can, however, exhibit normal cognition in the presence of A β plaques, indicating that they alone are not sufficient to cause dementia and may not be accurate biomarkers of severity of the disease.(9)

More recently, mitochondrial dysfunction has been proposed as a factor in the pathogenesis of AD (8, 10-12). Consistent evidence supports significant metabolic disruption that occurs early in the progression of AD, potentially presenting before the onset of clinical symptoms (13, 14). A significant source of energy is required for proper brain function, which in normal individuals is typically provided by glucose derived from carbohydrate consumed in the diet. Individuals with AD exhibit a consistent decrease in brain glucose utilization (15-19).

Support for the mitochondrial-related hypotheses for AD has increased based on the use of cytoplasmic hybrid (cybrid) techniques (20, 21). Cybrid cells are produced by fusing enucleated cells containing mitochondrial DNA (mtDNA) with nucleated cells replete of mtDNA (20). MtDNAs transfer to the nucleated cells, replicate and establish aerobic metabolism (20). Models in which cybrids containing mtDNA of platelets from patients with AD or MCI compared to age-matched healthy controls demonstrate significantly decreased respiratory metabolism in the AD cybrids (22-25). These findings suggest that mitochondria and mtDNA are complicit in bioenergetic deficits observed in AD.

It is not known whether the metabolic impairment observed in AD is cause or consequence in the pathogenesis of the disease, although many have hypothesized the

former. Nevertheless, there is great interest in mitochondrial and metabolic targeting in the treatment of AD (26). Manipulation of energetic substrates through diet may be a potentially effective therapeutic or preventive approach to AD (27).

Normal Brain Energy Metabolism

The brain demands 20% or more of total body energy (28, 29). In normal brain metabolism, glucose serves as the major cerebral energy substrate. The Western diet commonly contains 50-65% of total energy as carbohydrate (30). Carbohydrates from the diet are converted to glucose primarily destined for meeting energy metabolism demands. Glucose is transported across the endothelium of the blood-brain barrier via the non-insulin dependent glucose transporter, GLUT 1. It then enters either astrocytes via GLUT 1 or neurons via GLUT 3, which are not insulin dependent. Neuronal energy metabolism is the major focus of underlying brain energy metabolism, although some neuronal metabolism may depend on substrate production by the astrocyte (31). In the neuron, the inner-mitochondrial electron transport chain (ETC) is the primary source of cerebral ATP production. The ETC consists of five complexes (Complex I-V), which completely oxidize glucose to carbon dioxide and water and create an inner-mitochondrial proton gradient change that drives ATP production. A disruption in any complex of the ETC can cause serious energy perturbations in the brain energy flux.

Glucose Metabolism Impairment in AD

There is a clear link between AD and cerebral glucose utilization impairment (26). This impairment is exhibited early in AD and may even present prior to onset of AD

symptomology (13, 14). Positron emission tomography (PET), using fluorodeoxyglucose (FDG) as a marker, allows measurement of glucose uptake into brain tissue and subsequently provides insight into glucose metabolism in the brain known as the cerebral metabolic rate of glucose (CMRg) (32). Normal brain CMRg is approximately 100-120g/day (33). During the course of healthy aging, CMRg is known to decrease by 12-15% (34). Alzheimer's disease appears to have an even greater effect on CMRg. Compared to age matched older adults with normal cognition, mild AD patients exhibited a 20-25% global reduction in brain CMRg and regional reductions as high as 33% (34, 35). Hypometabolism of the primary systemic energy substrate could elicit cerebral energy crisis expediting neuronal deterioration and cognition impairment. Several factors have been investigated as major contributors to the hypometabolic state exhibited in AD.

In the brain, glucose uptake is primarily mediated by non-insulin dependent GLUT 1 and GLUT 3 transporters, both known to have decreased expression in AD (36, 37). Insulin-dependent Insulin Receptor and GLUT 4 are expressed in neurons of the hippocampus, a region integral to learning and memory in mammals (38). Glucose-mediated increases in plasma-insulin levels induce GLUT 4 translocation in the rat hippocampus, indicating an important role for insulin in hippocampal brain glucose metabolism (39, 40). Many metabolic conditions influence insulin sensitivity and are quite prevalent in the United States, including type 2 diabetes and obesity (41). Systemic and, in turn, regional cerebral reductions in insulin sensitivity could influence hippocampal glucose utilization (42).

Mitochondrial dysfunction is a leading theory for the pathology of AD. The mitochondrion houses the ETC and is the primary contributor of neuronal ATP. Alterations in the expression of mitochondrial DNA (mtDNA) appear to have a profound effect on ETC activity (26). In vitro studies using cells from both humans and mice exhibit common abnormalities in the mitochondria of AD, including downregulation of genes encoding for NADH dehydrogenase (complex I) and cytochrome c-oxidase (complex IV) of the ETC (43, 44). Furthermore, the brains of individuals with AD exhibit downregulation in expression of mitochondrial enzymes crucial for energy production (45). At this time, the cause of mitochondrial defects in AD is unclear. Inherited mtDNA is proposed as a determinant of baseline mitochondrial function (26). If defective mtDNA is inherited, the mitochondria have a decreased ability to produce ATP. Oxidative stress from reactive oxygen species (ROS) is also known to elicit damaging effects on mitochondria (46, 47). The mitochondria are large contributors to cerebral ROS production, which is typically reduced by local antioxidant systems prior to oxidative stress. If defects in the ETC exist, mitochondrial production of ROS is likely upregulated and could potentially lead to further ROS-mediated ETC disruption (48). Evidence indicates that inhibited mitochondrial function also likely influences upregulation of A β deposition (26), which has been shown to deposit in the mitochondria of the neurons and further inhibit the ETC (49). As multiple factors play a detrimental role in mitochondrial inhibition observed in AD, disease pathogenesis and progression is likely cyclical.

Dietary Factors and AD

As it becomes more clear that metabolism is either a factor in AD pathology or affected by its development, interest in the relationship between diet and AD has increased.

Studying the role of nutrition in disease states can be difficult. Studies often focus on the relationships of a single or handful of nutrients to outcomes, which is valuable, but may exclude interactive or synergistic effects of foods and nutrients. For the full scope of dietary impact, in addition to solitary nutrients, identification of dietary patterns can explore the synergistic effects of foods and nutrients and account for potential food interrelatedness (30, 50). Although single nutrients have been studied with mixed reports in AD epidemiological and clinical trials, epidemiological studies of dietary patterns have been most compelling and will be the primary focus of this review.

The Western diet pattern was originally described by Hu et al. through the use of principal components analysis (PCA) (30). Consisting of high intake of red meat, refined grains, processed meat, high-fat dairy products, dessert, sugary beverages, eggs, french fries and potatoes, the Western diet is predictive of type 2 diabetes and other conditions of impaired peripheral metabolism (51, 52) that are risk factors for AD as discussed below. A Western dietary pattern is also strongly correlated with AD incidence (53) and has negatively affects brain structure, neuronal generation and cognitive function (54-56).

The Mediterranean dietary pattern stands in clear contrast to the Western dietary pattern with high intake of fruits, vegetables, legumes and cereals; moderate consumption of oily fish and dairy; and low consumption of meat, sugar and saturated

fat. Most dietary fat in this diet pattern comes from olive oil. Wine is consumed in moderation with meals (57). Epidemiological data suggest that adherence to the Mediterranean diet is inversely correlated with insulin resistance (58), inflammation that causes oxidative stress (59, 60) and risk of AD (57, 61).

Researchers at Rush University identified the Mediterranean-Dietary Approaches to Stop Hypertension Intervention for Neurodegenerative Delay (MIND diet) through epidemiological data (62). The MIND diet is a dietary pattern that combines the Mediterranean dietary pattern and the Dietary Approaches to Stop Hypertension diet (DASH diet) (62). AD risk appears to be diminished in a step-wise fashion dependent on an individual's MIND diet adherence score (62). The MIND diet focuses, particularly, on 15 food components that are simply broken into "brain health food groups" and "unhealthy food groups" (Table 1).

Table 1 MIND Diet Food Groups

Brain Healthy Food Groups	Unhealthy Food Groups
Green leafy vegetables	Red meats
Other vegetables	Butter and stick margarine
Nuts	Cheese
Berries	Pastries and sweets
Beans	Fried or fast food
Whole grains	
Fish	
Poultry	
Olive oil	
Wine	

Novel A β Imaging and Relationship with Nutrients

In vivo positron emission tomography (PET) imaging for quantification of cerebral A β deposition as an objective outcome biomarker in AD studies is a recent trend (63).

A β can be measured in PET images through administration of either ^{11}C Pittsburgh Compound B (PiB) or Florbetapir (^{18}F), radiopharmaceutical compounds that bind A β (64). Approximately 30% of cognitively normal older adults exhibit elevated amyloid burden while the prevalence of elevated amyloid burden in MCI and AD is 60% and 90%, respectively (63).

An emerging field of study, few studies relate nutrients to PET identified amyloid burden. Mosconi et al. (65) published a pilot study that investigated the relationship between nutrient intake and amyloid burden in 49 non-demented adults. Higher intakes of vitamin B12, vitamin D and omega-3 fatty acids were associated with attenuated deposition of A β . Although the study used exploratory statistical procedures, it serves as proof of concept for investigating the relationship of diet and amyloid burden. Berti et al. (66) investigated the relationship between nutrient patterns and amyloid burden in 52 cognitively normal adults. Thirty-five nutrient variables were used as input into principal components analyses and 5 distinct dietary nutrient patterns were identified. An inverse relationship was exhibited between amyloid burden and the dietary pattern with high loading coefficients for vitamin B12, vitamin D and zinc, suggesting a role for these nutrients, potentially synergistically, in preventing A β accumulation.

Further suggesting a relationship between A β processing and nutrition, two studies investigated correlation between serum nutrient status and amyloid burden. In a cohort of 73 cognitively normal older adults, Morris et al. demonstrated that elevated fasting serum glucose was strongly associated with elevated amyloid burden (67). Yassine et al. showed a significant inverse relationship between serum docosahexanoic

acid status, an omega-3 fatty acid commonly found in fatty fish, and cerebral A β burden in a cohort of 61 older adults with either normal cognition or MCI (68).

The clinical relevance of A β is not precisely defined, but elevated accumulation is a known risk factor and likely part of the complex pathology of AD (69). Cerebral amyloid quantification techniques have opened the door to a better understanding of factors that affect A β processing and, in turn, risk of AD. Mounting evidence suggests a possible role for nutrition in amyloid protein processing, however, we've only scratched the surface of potential for investigating these relationships.

Impaired Glycemia/Insulin Resistance and Brain Metabolism

Metabolic disorders such as type 2 diabetes are known risk factors for AD. Individuals with type 2 diabetes (70-74) and elevated blood glucose (70) are at higher risk of dementia and experience more rapid progression from MCI to AD (75). Peripheral hyperglycemia and insulin resistance are believed to promote cerebral glucose hypometabolism (76-79). Slight elevation of fasting blood glucose in cognitively normal individuals is associated with diminished glucose metabolism in brain regions highly affected in AD (77-79).

Cerebral hypometabolism is believed to be one of the mechanisms involved in upregulated cerebral A β deposition seen in AD pathology (80). In a mouse model of AD, inducing acute hyperglycemia through intravenous flow of dextrose increased A β in the interstitial fluid of the brain (81). Late middle age adults with insulin resistance had increased regional cerebral A β burden while cognitively normal older adults with impaired fasting glucose also demonstrate increased regional cerebral A β burden (67,

82). Because neuronal protein processing requires a steady flux of energy, hypometabolism elicited bioenergetic deficits likely contribute to impaired processing of A β and plaque accumulation (8). The relationship between cerebral glucose hypometabolism and A β processing may be cyclical in that downregulated brain glucose metabolism could potentiate A β burden and further intensify cerebral hypometabolism (83).

Sugar, Glycemic Index and Glycemic Load in AD

Glucose metabolism is severely downregulated in and prior to onset of AD. Accumulating evidence also points to a role for conditions of altered metabolic status as a risk factor for AD. Despite existing links of glucose metabolism with A β processing and influence of dietary intake on glucose metabolism status, very little work has been done to assess the relationships of sugar and highly glycemic carbohydrates with AD.

Dr. David Jenkins and colleagues developed the glycemic index (GI) in 1981, a scale that scores the postprandial glycemic response of carbohydrate containing foods relative to a reference of glucose or white bread (84, 85). GI scores represent the area under a 2-hour glucose response curve following a 12 hour fast and 50g ingestion of a carbohydrate containing food (85). On a scale of 0-100, foods with a GI greater than 70 are considered high glycemic foods, while those between 56-74 are considered medium glycemic foods and those less than 55 are considered low glycemic foods.

Walter Willett first proposed glycemic load (GL) in 1997 (86). GL is intended to describe the anticipated glycemic effect of carbohydrate consumption using the GI and taking into account the quantity of carbohydrate consumed. GL is calculated as GL =

(GI of individual food x grams carbohydrate per serving)/100. Studies demonstrated that GL consumed through the day can be summed to establish a cumulative daily GL (87) and that the GL was predictive of the glycemic response of ingestion of a mixed macronutrient meal (88).

It is well established that diets rich in high GI foods, characterized by intake of processed carbohydrates and sugar, are strongly associated with impaired glucose metabolism, including insulin resistance and type 2 diabetes (86, 89-95). Intake of carbohydrates with a high GI elicits sharp postprandial spikes in blood glucose and requires a greater insulin demand for glucose shuttling. Diets consisting of carbohydrate with a high GI and GL are correlated with fasting hyperglycemia and hyperinsulinemia as well as decreased insulin sensitivity (96). This is important because individuals with type 2 diabetes are significantly more likely to develop dementia and experience more rapid progression once dementia begins (75).

We must look to rodent models to evaluate the role of sugar intake in AD risk. Inducing acute hyperglycemia in mice through intravenous flow of dextrose increased A β in the interstitial fluid of the brain (81). This suggests that acute hyperglycemia from the consumption of processed carbohydrates and sugars could potentially mimic this effect. When fed a high sugar and high fat diet, mice develop metabolic syndrome and express upregulated A β deposition and tau phosphorylation (97). Dietary-induced insulin resistance in rodents through high intake of sugar or high fructose corn syrup resulted in elevation of A β burden and significant impairment of cognition (98-100). These studies and others suggest that acute increases in insulin and insulin signaling through the consumption of high glycemic foods may change A β levels in the brain

through proteolysis by insulin-degrading enzymes (101) and/or A β clearance from the brain (102).

Ketone Metabolism

Ketone bodies result from the mobilization of fatty acids to the liver where they undergo conversion from fatty acids to ketone bodies. There are three ways in which serum levels of ketone bodies are elevated, through 1) increased mobilization of endogenous fatty acids due to prolonged fasting (103), 2) adherence to a ketogenic diet (KD) (104), and 3) intake of ketogenic agents, such as medium-chain triglycerides (MCT) or exogenous ketone body substrates (105, 106). From a therapeutic standpoint, it is common practice to combine the ketogenic diet with intake of ketogenic agents (i.e. a ketogenic diet supplemented with MCT) (107).

Ketosis as a result of fasting and following the KD are relatively similar mechanistically, i.e., ketosis is the result of decreased glucose availability and increased mobilization of fatty acids. Ketogenic agents have different mechanisms. MCT induced ketogenesis is unique in that MCTs are rapidly absorbed by the enterocyte and enter the portal vein gaining direct access to the liver, a key distinction from short and long chain fatty acids which first enter the lymphatic system. MCT is also unique in that it is not dependent upon carnitine activation for beta-oxidation in the liver, resulting in rapid ketogenesis. Exogenous ketones, often in the form of ketone esters, are bound ketone bodies that are hydrolyzed and absorbed intact resulting in elevated serum ketone levels. Ketogenic agents alone acutely raise serum ketone levels until the ketone bodies are cleared through metabolic pathways and serum levels normalize.

The liver is estimated to have the capacity to synthesize 185g of ketone bodies per day (108). Hepatic mitochondria convert acetyl-CoA from beta-oxidized fatty acids to the ketone bodies acetoacetate, β -hydroxybutyrate and, to a lesser extent, acetone (109). Ketone bodies translocate to the mitochondria of extrahepatic tissue where they are retro converted to acetyl-CoA and enter aerobic respiration pathways (109). The brain readily uses ketones as a fuel source in prolonged fasting. The two major energy-contributing ketones, acetoacetate and β -hydroxybutyrate, can provide up to 60% of the brain's functional energy requirements (110). During periods of low levels of serum insulin, fatty acids are mobilized and transported to the liver where they are metabolized to ketone bodies that are released to the blood. Ketones transport across the blood brain barrier and the cerebral metabolic rate of ketones (CMR_k), a measurement of brain ketone utilization, is highly related to plasma ketone concentration (111). High plasma ketone concentration influences neurons and astrocytes to increase the expression of monocarboxylic acid transporters, which are responsible for the transport of ketones into these cells and, ultimately, increase cerebral cellular ketone uptake (112).

Ketogenic Diet

Dr. Russell Wilder at the Mayo Clinic first wrote about the ketogenic diet in 1924 (113). Until recently, the ketogenic diet has been considered nearly exclusively in the realm of seizure control therapy in Epilepsy. The typical American diet differs greatly from the ketogenic diet in that it is typically defined by high carbohydrate consumption (50-65% of energy) while the ketogenic diet is very high in fat and commonly reduces

carbohydrate to less than 10% of energy. Through the years, the diet has taken on several different iterations with varying levels of ketogenic potency. Typically, the diet is referenced as a ratio of grams of fat to grams of carbohydrate and protein combined.

4:1 Ketogenic Diet. The classic ketogenic diet has long been the standard for ketogenic therapy in epileptic children. This version of the diet consists of 90% of energy as fat, 2% of energy as carbohydrate and 8% of energy as protein.

The 3:1 Ketogenic Diet. The 3:1 diet is very similar to the classic 4:1 ketogenic diet with 87% of energy from fat, 4% of energy as carbohydrate and 9% of energy as protein.

The 2:1 Ketogenic Diet. The 2:1 ketogenic diet is slightly less restrictive than its 4:1 and 3:1 counterparts. It is characterized by 82% of energy from fat, 8% of energy from carbohydrate and 10% of energy as protein.

The 1:1 Ketogenic Diet. The 1:1 ketogenic diet is the least restrictive of the ketogenic ratios. This ratio consists of 70% of energy from fat, 10% of energy from carbohydrate and 20% of energy from protein. Many of the more liberal iterations of the ketogenic diet use the 1:1 ketogenic ratio as their dietary basis.

Table 2 Classical Ketogenic Diets

	4:1 KD	3:1 KD	2:1 KD	1:1 KD
Fat % (g)	90% (200g)	87% (193g)	82% (182g)	70% (156g)
Carbohydrate % (g)	2% (10g)	4% (20g)	8% (40g)	10% (50g)
Protein % (g)	8% (40g)	9% (45g)	10% (50g)	20% (100g)

Grams of macronutrients based off reference of 2000 calories

MCT-Supplemented Ketogenic Diet. Based on the macronutrient distribution from the 1:1 ketogenic diet, this version aims to provide 30-40% of the total fat consumed as

MCT. Due to the ketogenic nature of MCT, the MCT-supplemented ketogenic diet allows individuals to be more liberal with their carbohydrate and protein intake.

Adherence to this diet has been shown to be as effective at halting seizures as the classic ketogenic diet and to result in similar peak ketone production (114).

Modified Atkins Diet. The Modified Atkins Diet (MAD), designed by physicians at Johns Hopkins Hospital, is a less restrictive version of the ketogenic diet (115). This version of the diet is primarily based on a 1:1 ketogenic ratio. In its use as an epilepsy treatment, the initiation of the diet limits patients to 10 g of carbohydrate per day gradually increasing to the 1:1 ratio over the subsequent months (116). In epilepsy, MAD has been shown to be more feasible than classical ketogenic diet approaches with very similar seizure control (117).

There is growing interest in the potential use of the ketogenic diet as a therapy outside of epilepsy. The ketogenic diet is linked to many biological pathways (i.e. fatty acid oxidation, oxidative stress, inflammation, etc.) suggesting that it could be an approach to favorably manipulate bioenergetics in several neurological diseases (118).

Can Ketone Bodies Compensate for Bioenergetic Deficit in AD?

This review previously outlined the bioenergetic deficit caused by impaired glucose metabolism in AD. It has been proposed that the presence of ketone bodies could compensate for this deficit (119, 120). Recent studies have investigated the potential role for ketones and have constructed a compelling argument for this very concept.

Castellano et al. (35) designed a study to test whether ketone metabolism remains intact in patients with AD. In accordance with consistent previous findings, a cohort of mild AD patients was shown by FDG-PET to have significantly impaired cerebral glucose uptake when compared to age matched healthy adults using CMRk measured by PET using radioactively marked acetoacetate (C-AcAc), sans ketogenic intervention, was the same in both groups.

An additional study performed by the same group tested the hypothesis that increasing the availability of ketones would affect CMRk in adults (121). A 4.5:1 ratio liquid ketogenic diet was provided to 10 adults across the age span for 4 days. Ketosis was achieved by the participants with an 8-fold elevation of serum ketone levels by day 4. CMRk was elevated to 33% of total brain energy metabolism while CMRk was reduced by 20%, indicating a significant switch from cerebral metabolism of glucose toward ketone metabolism.

Whether or not the CMRk response to ketone availability is induced in individuals with AD is still to be determined. A current study in progress suggests that AD brains may even exceed the CMRk response seen in healthy adults (Cunnane or Courchesne-Loyer Abstract).

Ketogenic Diet/Ketones in AD

The potential use of brain ketone delivery as a treatment for AD was proposed in 1989 (119). It is desirable to know if systemic ketosis could potentially serve as a therapeutic intervention in AD. Many reviews have proposed the concept of ketones as

a possible treatment in AD; however, to date, very few studies have evaluated the feasibility and efficacy of ketosis as an AD treatment.

Yao et al. investigated the effect of ketosis in the female triple-transgenic AD mouse model. The experimental group received a diet consisting of 0.04% 2-Deoxy-D-Glucose (2-DG) for 7 weeks while the control group received a regular chow diet (122). 2-DG has a structural resemblance to glucose; however, 2-DG is unable to undergo phosphorylation, which competitively inhibits glucose metabolism and promotes elevation of ketone bodies. Exposure to the 2-DG diet for 7-weeks induced a significant increase in serum beta-hydroxybutyrate, sustained mitochondrial function and significantly reduced oxidative stress. An inverse correlation between beta-hydroxybutyrate levels and brain amyloid levels was also demonstrated.

Henderson et al. tested the clinical potential of beta-hydroxybutyrate in AD in a randomized, double-blind clinical trial in which 86 participants received caprylic triglyceride and 66 participants received a placebo (105). Caprylic triglyceride is a medium chain triglyceride (MCT) that is converted to ketone bodies in the liver. Two hours after caprylic triglyceride consumption, serum beta-hydroxybutyrate levels increased approximately 4-fold. By study day 90, serum levels rose from about 0.1 mM to 0.40 mM in the participants receiving caprylic triglyceride. On day 45 the active treatment group's Alzheimer's Disease Assessment Scale-Cognition Subscale (ADASCog) score improved by 0.31 points and was significantly better than the placebo group's score, which worsened by 1.23 points. The treatment group's ADASCog scores also improved on day 90, although the improvement was not statistically significant. Participants who expressed the APOE4 negative genotype receiving caprylic

triglyceride demonstrated significantly better ADASCog scores than the placebo group at 45 and 90 days with differences of 5.73 points and 4.39 points, respectively.

Krikorian et al. randomized 23 MCI participants to either a low carbohydrate or high carbohydrate diet (123). Twelve participants were assigned to the low carbohydrate diet that limited daily carbohydrate consumption to 5-10% of total caloric intake while 11 participants consumed a diet that consisted of ~50% carbohydrate. At the end of the 6-week intervention, urine ketones rose from 0 mg/dL to 5.4 mg/dL in the carbohydrate restriction group. Cognition was evaluated using the paired associate learning test. The low carbohydrate treatment group significantly improved their cognition scores from baseline to 6 weeks. Furthermore, a positive correlation between urine ketone levels and memory test improvement was observed. The eleven participants who maintained a high carbohydrate diet showed no change in urine ketones and no cognitive improvement.

A case study published in 2015 reported that dosing of 28.7 g of ketone ester three times per day effectively raised serum ketone levels and was well tolerated (106). Although no clinical assessment of cognition was performed, the case review reported that the patient exhibited improved behavior and cognition over the course of 20 months.

A review from 2012 compiled relevant evidence regarding ketosis and oxidative stress (124). Oxidative stress is believed to play a significant role in the pathogenesis of AD. Although the body of evidence is limited, evidence infers that, in rats, the ketogenic diet improves oxidative stress status by decreased ROS, upregulation of glutathione and potential down downregulation of key inflammatory pathways.

Although limited data involving the ketogenic diet or ketone therapies in AD exist, the current body of evidence supports the premise that these interventions are worthy of further investigation. While a previous study investigated carbohydrate restriction in MCI, at this point, it is unclear whether individuals with AD are capable of following the ketogenic diet or if following the diet would improve AD symptomology. Addressing these questions is the purpose of the research presented in the ketogenic portion of this dissertation.

Research Questions and Gaps in Literature

1.) How does intake of sugar and foods with a high glycemic index affect AD pathology, primarily A β accumulation?

There has been a great effort to elucidate the mechanisms of glucose metabolism's influence on brain hypometabolism and amyloid processing, yet very little literature connecting dietary intake to objective measures for AD risk exists. I hypothesize that that sugar intake and glycemic load intake is positively correlated with cerebral amyloid burden.

2.) What is the relationship between intake of a High Glycemic Load Diet pattern and accumulation of A β ?

Study of dietary patterns in relation to various outcomes has become more common. Evaluation of eating patterns is a more comprehensive manner of looking at dietary intake than solitary nutrients. Principal components analysis was used to identify actual dietary patterns within our dataset. The first pattern was strongly associated with

glycemic load and sugar intake, therefore it was named the High Glycemic Load Diet pattern. I hypothesize that, like my previous hypothesis for glycemic load and sugar intake, the High Glycemic Load Diet pattern will positively correlate with cerebral amyloid load.

3.) Is the MCT-supplemented ketogenic diet feasible in patients with AD?

Although the Krikorian study investigated the feasibility of carbohydrate restriction in MCI, no studies have been designed to evaluate the feasibility of the ketogenic diet in AD. Demonstrated feasibility of KD in patients with AD would provide justification for evaluating efficacy of KD as a treatment option for AD patients.

4.) Does following a ketogenic diet elicit cognitive benefit in patients with AD?

While reviews and editorials have speculated that ketones may overcome bioenergetic deficits observed in AD, however, there are yet to be any clinical trials to evaluate the cognitive efficacy of KD in patients with AD. In conjunction with feasibility, demonstration of potential cognitive benefit of KD in patients with AD could further justify and provide the knowledge necessary to power a KD efficacy trial in AD.

Chapter Two: Subjects and Methods

Two studies have been considered for the purpose of answering the questions proposed in this dissertation. The following will address the methods from both studies.

Alzheimer's Prevention through Exercise (APEX)

The Alzheimer's Prevention through Exercise (APEX) is a randomized controlled exercise trial intended to examine the effects of exercise on AD biomarkers and cognition. At screening, potential participants undergo Florbetapir F18 PET imaging to assess and quantify cerebral amyloid status. Eligible participants with elevated amyloid enroll in the APEX study. Potential participants that are non-elevated enter the Alzheimer's Prevention Program study, an imaging sub-study of APEX with an enrollment goal of 400 cognitively normal older individuals. Data from the screening visit (prior to APEX intervention) were analyzed cross-sectionally including both amyloid elevated and non-elevated participants.

Eligibility

Prior to enrollment in APEX or APP, participants were enrolled in the KU Alzheimer's Disease Center Registry. The registry is intended to develop a well-defined pool of recruitable individuals for AD research studies. All possible recruits were eligible for APP if they met the following criteria: a) age 65 or older; b) CDR of 0 (no dementia) (125) as assessed by a cognitive battery (126), clinical assessment and interviews with potential participant family members (all clinical assessments were reviewed at a consensus diagnosis conference); c) no clinically significant depression (Geriatric Depression Scale score at sub-study Visit 1 must be 5 or less); d) no clinically

significant anxiety (Beck Anxiety Index at sub-study Visit 1 must be 16 or less) and e) sedentary or underactive based on the Telephone Assessment of Physical Activity (127) (score of 4 or less).

Individuals were excluded from participation of this study if they had a) clinically significant hepatic, renal, pulmonary, metabolic, endocrine, psychiatric or medical disturbances as indicated by history, which, in the opinion of the investigator, posed a potential safety risk to the subject; b) history of relevant severe drug allergy or hypersensitivity; c) received a radiopharmaceutical for imaging or therapy within the 24 hours prior to the imaging session for this study or d) current or recent participation in any procedures involving radioactive agents such that the total radiation dose exposure to the subject in any given year would exceed the limits of annual and total dose commitment set forth in the US Code of Federal Regulations (CFR) Title 21 Section 361.1.

Assessment of Dietary Intake

At visit 1, usual dietary intake was assessed using the web-based National Cancer Institute Diet History Questionnaire II (DHQII) (<https://epi.grants.cancer.gov/dhq2/>) which is a semi-quantitative, 134 food item food frequency questionnaire. Participants were asked to report the average frequency of consumption and portions of food items for the previous year. Estimated nutrient data were quantified using the NCI Diet*Calc software (<https://epi.grants.cancer.gov/dhq2/dietcalc/>).

Florbetapir F18 PET Image Acquisition

Florbetapir F18 PET scans were acquired on a GE Discovery ST-16 PET/CT scanner at visit 2. Vital signs were taken in a supine position immediately prior to administration of florbetapir F18. A 370 MBq bolus injection of florbetapir F 18 was administered and two PET brain frames of 5 minutes in duration were acquired continuously approximately 50-minutes post-injection. PET acquisitions were reconstructed immediately after scan completion. If any motion was detected, a second continuous scan was acquired. Subjects were observed continuously for signs of adverse events or serious adverse events.

Assessment of Cerebral Amyloid Burden

Florbetapir F18 PET images were analyzed both qualitatively and quantitatively. Qualitative analysis was performed by 3 trained raters (either a radiologist or nuclear medicine physician) blinded to the subject diagnosis and reported images as either “elevated” A β levels (AD-like) or “not-elevated” A β levels (not AD-like). The final determination whether images were elevated or non-elevated was determined by majority (i.e., ≥ 2 raters in agreement). Quantitative analysis was processed using MIMneuro (MIM Software Inc., United States) software to measure mean standard uptake values (SUV) for target areas including the anterior cingulate, posterior cingulate, precuneus, inferior medial frontal, lateral temporal and superior parietal cortex and a reference region consisting of the cerebellum using a proprietary algorithm. Standard uptake value ratios (SUVR) for each cortical target area was calculated relative to the cerebellum.

Cognitive Assessment

All participants completed a standard battery of neuropsychological tests that included the Mini-Mental State Exam (MMSE), the Wechsler Adult Intelligence Scale – Revised (WAIS-R) Digit Symbol, Trail Making Test A, Trail Making Test B, Category Fluency (animals and vegetables), the Stroop Color-Word Interference Test, the WAIS-R Block Design and the total free recall score from the Free and Cued Selective Recall Test (126).

Ketogenic Diet Retention and Feasibility Trial

Eligibility

Individuals were eligible for this study if they 1) met the criteria for *MCI Due to AD, Mild AD or Moderate AD*; 2) had a study partner; 3) had a BMI greater than 21 kg/m²; 4) had serum electrolytes, liver function tests (LFTs) and cholesterol levels within normal limits and 5) spoke English as a primary language. Individuals were ineligible if they reported any of the following criteria: if they 1) did not have a study partner to assist in implementation and maintenance of the ketogenic diet; 2) consumed greater than 2 drinks of alcohol per day; 3) reported serious medical risk such as insulin-dependent diabetes, cancer, or recent cardiac event (i.e. heart attack, angioplasty, etc.) or 4) had a BMI of 21 kg/m² or less.

Anthropometrics

Participants were weighed on a calibrated scale in light clothing without shoes and weight recorded to the nearest 0.1 lb. Height was measured using a stadiometer without shoes and recorded to the nearest 0.1 cm. All anthropometric data were obtained and recorded by the nursing staff in the KU Clinical Translational Science Unit (CTSU).

Body Composition

Dual-energy x-ray absorptiometry (DEXA) scans were performed by the Exercise Physiology Lab located in the CTSU prior to diet initiation and at the end of the diet intervention. Total body tissue quantitation was obtained via a total body scan, which provided output for 3 tissue compartments; lean tissue, fatty tissue and bone. Lunar Encore software (Version 13.6) used to quantify tissue of each compartment.

Blood Collection and Assays

Fasting serum samples were collected and processed by nurses in the CTSU. Laboratory values collected just before the start of the intervention and at its completion included serum electrolytes, including calcium, chloride, magnesium, phosphorus, potassium and sodium; liver function tests (LFTs), including AST, ALT and ALP; renal labs, including BUN and creatinine; and a full lipid panel, including total cholesterol, LDL, HDL and triglycerides. Plasma insulin levels and β -hydroxybutyrate were collected at one-month intervals. KU Medical Center Clinical Laboratory analyzed all assays with respective ELISA kits.

Plasma insulin and glucose was measured at baseline and at the end of the diet intervention. We calculated Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) values for each participant. Whole body insulin sensitivity (HOMA2-IR) was calculated using HOMA2 Calculator (v. 2.2.3; University of Oxford, United Kingdom).

Electrocardiogram (ECG)

Electrocardiography was recorded at Baseline, Month 1 and Month 2 of the dietary intervention. We monitored for any changes in Q-wave activity. Nurses in the CTSU obtain all electrocardiography and the recordings were analyzed by the study physicians and trained staff.

Cognitive Assessment

Cognitive performance was assessed using the cursory mini-mental state exam (MMSE) and the more detailed AD Assessment Scale cognitive subscale (ADASCog). The MMSE is a 30-point survey designed to measure participant orientation, immediate recall, attention and calculation, recall and various aspects of language (128). The ADASCog consists of 11 tasks and measures the disturbances of memory, language, praxis, attention and other cognitive abilities that are often referred to as the core symptoms of AD (129). Experienced KU ADC staff conducted cognitive testing at three time points: 1) baseline, 2) at diet conclusion and 3) one month following diet conclusion.

Assessment of Ketones

Participants recorded urinary acetoacetate results using Ketostix (Bayer, Germany) each evening. The observed color changes indicated the presence of no (~0 mg/dL), trace (~5 mg/dL), small (~15 mg/dL), moderate (~40 mg/dL), high (~80 mg/dL), or very high (~160 mg/dL) acetoacetate. Participants recorded urinary ketone results in a diary provided by study personnel.

Dietary Intake

Dietary intake was assessed by 3-day food records. Participants recorded 3 consecutive days of intake; 2 weekdays and one weekend day. Baseline food records were completed prior to starting the ketogenic diet in order to estimate normal dietary intake. Food records completed at the end of the first and second months reflected dietary intake while consuming the ketogenic diet. Data from the 3-day food records were entered into the Nutrition Data System for Research (NDSR, v. 2016) software.

Statistical Analyses

Analyses were performed using R (v. 3.3.2; R Foundation, Vienna, Austria). All statistical analyses were two-sided with statistical significance set at $p \leq 0.05$.

Dietary Glycemic Measures and Cerebral Amyloid Burden

Linear regression models were used to investigate the relationships between dietary glycemic measures (carbohydrate, sugar and glycemic load) and regional cerebral amyloid burden (SUVR) in 126 cognitively normal older adults. Residual

analyses were performed on all dependent variables to assess applicability of linear regression and normality was assessed using the Shapiro-Wilk test for normality. Dependent data with non-normally distributed residuals were log transformed. All analyses were controlled for age and gender.

High Glycemic Load Dietary Pattern and Cerebral Amyloid Burden

Dietary patterns were produced using principal components analysis (PCA). The NDSR output consolidates a possible 7,752 foods consumed by participants into 32 food variables of the *My Pyramid Equivalents Database 2.0* (MPED 2.0) (130). MPED 2.0 variables were included in the PCA correlation matrix and rotated with the varimax rotation method. The first rotated factor, describing 13.7% of the variability in the data, was retained from the factor analysis. This factor (dietary pattern) was regressed against energy, fat, protein, carbohydrate and glycemic load. The dietary pattern was named the High Glycemic Load Dietary pattern because it was associated with carbohydrate, sugar and most correlated with glycemic load.

The relationships between the High Glycemic Load Dietary pattern with global and regional amyloid burden were assessed using linear regression. Analyses were controlled for age, gender, BMI and education level.

Dietary Measures/Patterns and Cognition

Linear regression models were used to investigate the relationships between dietary glycemic measures (carbohydrate, sugar and glycemic load) and the High Glycemic Load Dietary pattern with individual cognitive tests from the cognitive battery

and a computed global cognitive score. Residual analyses were performed on all dependent variables to assess applicability of linear regression and normality was assessed using the Shapiro-Wilk test for normality. Dependent data with non-normally distributed residuals were log transformed. Analyses were controlled for age, gender, BMI and education level.

MCT-KD Feasibility

Feasibility of the ketogenic diet was determined, in large part, by descriptive statistics. Normality of the dependent variables was assessed through Q-Q visualization of residuals models. Paired t-tests were utilized to analyze differences in dietary macronutrient intake prior to and during diet intervention. Changes in serum ketone status during the dietary intervention were analyzed using the non-parametric Friedman test with Conover post-hoc analyses.

Changes in Cognition

Pre and post dietary intervention cognition scores were analyzed using repeated measures ANOVA. Assumptions for ANOVA were evaluated by visualization of Q-Q plots of residual models.

Chapter Three: High Glycemic Diet is Associated with Cerebral Amyloid Burden in Cognitively Normal Older Adults

Abstract

Objective: Examine the relationship of dietary glycemic measures with cerebral amyloid burden and cognitive performance in cognitively normal older adults.

Methods: We performed cross-sectional analyses of dietary glycemic measures (high glycemic load diet pattern [HGLDiet], sugar intake, carbohydrate intake and glycemic load) with cerebral amyloid burden (measured by florbetapir F-18 PET) and cognitive performance in 128 cognitively normal older adults screened for the University of Kansas Alzheimer's Prevention through Exercise trial.

Results: Amyloid was elevated in 25.4% (n=32) of subjects. Adherence to an HGLDiet pattern was significantly higher in elevated subjects ($p=0.015$). The HGLDiet pattern was positively associated with amyloid burden both globally and in all regions of interest independent of age, gender, and BMI (all p -values ≤ 0.001). Individual dietary glycemic measures (sugar intake, carbohydrate intake and glycemic load) were also positively associated with global amyloid load and nearly all region regions of interest independent of age, gender and BMI (p -values ≤ 0.05). Cognitive performance was associated only with daily sugar intake, with higher sugar consumption associated with poorer global cognitive performance (Global Composite and Mini-Mental State Exam) and performance on subtests of Digit Symbol, Trailmaking B, and Block Design controlling for age, gender, and education.

Conclusions: A high glycemic diet is associated with greater cerebral amyloid burden, suggesting diet may be a potential modifiable risk factor for cerebral amyloid accumulation.

INTRODUCTION

Alzheimer's disease (AD) is the most common form of dementia, affecting more than 1 in 8 Americans over the age of 65 and costing the American economy over \$385 billion per year (2). AD prevalence is projected to increase to nearly 14 million by the year 2050 (2). As disease modifying therapies that slow decline in symptomatic patients are currently lacking, an interest in identifying approaches to prevent or delay AD onset has emerged (131). It is believed that lifestyle behaviors, including diet, could modify AD risk and that diet interventions could be used to reduce AD risk (132).

Recent studies demonstrate impaired glucose metabolism and peripheral hyperglycemia associate with AD risk. For instance, individuals with type 2 diabetes (71, 72) and elevated blood glucose (70) are at higher risk of dementia and experience more rapid progression from mild cognitive impairment (MCI) to AD (75). Peripheral hyperglycemia and insulin resistance are also believed to promote cerebral glucose hypometabolism as evidenced by PET imaging studies (76-79). Cerebral hypometabolism itself has been implicated in cerebral amyloid-beta ($A\beta$) deposition, which manifests in the form of the extracellular plaques (80). Further, a recent study demonstrated impaired fasting glucose associates with increased regional cerebral $A\beta$ burden in a cohort of cognitively normal adults (67).

Postprandial glycemia and insulin secretion are highly affected by the amount and type of carbohydrate consumed in the diet (133). Dietary intake of a high glycemic load, which can be characterized by a high intake of processed carbohydrate and sugar, elicits sharp spikes in peripheral glucose and insulin secretion. Diets with high in glycemic load have been strongly linked to impaired glucose metabolism and increased

risk of type 2 diabetes (96), which may also implicate diet as a modifiable behavioral factor that affects amyloid aggregation. Assessment of the association between dietary components and patterns known to affect glucose metabolism and A β deposition could help further elucidate their relationship with AD risk.

Despite recognized relationships between glucose metabolism and A β processing (67), as well as an appreciation for the fact that diet affects glucose metabolism (96), potential correlations between high dietary glycemic intake and cerebral amyloid burden remain relatively unexplored. In this cross-sectional study, we examined whether a high glycemic diet – as measured by a survey-based assessment of adherence to a High Glycemic Load diet pattern and estimates of daily carbohydrate intake, sugar intake, and glycemic load – associates with global and regional cerebral amyloid burden derived by florbetapir F-18 positron emission tomography (PET).

METHODS

Study Design

We examined cross-sectional data collected from individuals screened for the University of Kansas Alzheimer's Prevention through Exercise [APEX] trial to assess the association of dietary glycemic measures with regional cerebral amyloid burden. The APEX study is a randomized trial examining the effects of aerobic exercise on AD biomarkers (amyloid burden and MRI volumetrics) and cognitive decline in cognitively normal older adults 65 years and older (NCT02000583) conducted at the University of Kansas Alzheimer's Disease Center. Only screening or baseline data (i.e., prior to any intervention) was used for these analyses.

Subjects

Data were available on 128 cognitively normal, sedentary participants age 65 and older that screened for the University of Kansas Alzheimer's Prevention through Exercise (APEX) study. Participants were assessed by a trained clinician and performed a battery of cognitive tests (126) to exclude the presence of mild cognitive impairment or dementia syndromes. The trained clinician interviewed the participant and their study partner (usually a spouse or child) to assess for evidence of clinical decline and to complete a Clinical Dementia Rating (CDR) (125). Clinical and cognitive data were reviewed at a consensus diagnosis conference and eligible participants were CDR 0 (no dementia) and also without clinically significant deficits in their cognitive test performance. Participants were sedentary or underactive based on the Telephone Assessment of Physical Activity (127) (score of 4 or less) and willing to participate in a 52 week exercise intervention. Exclusion criteria for the APEX study included clinically significant depression or anxiety, insulin-dependent diabetes, uncontrolled hypertension, or recent history of major neuropsychiatric, musculoskeletal, or cardiorespiratory impairment in the last 2 years. The study protocol was approved by the Institutional Review Board at the University of Kansas Medical Center. Informed consent was obtained from all study participants according to institutional guidelines.

Dietary Intake Assessment

Usual dietary intake was assessed using the web-based National Cancer Institute Diet History Questionnaire II (DHQII) (<https://epi.grants.cancer.gov/dhq2/>) which is a semi-quantitative, 134 food item food frequency questionnaire. Participants

were asked to report the average frequency of consumption and portions of food items for the previous year. Estimated nutrient data were quantified using the NCI Diet*Calc software (<https://epi.grants.cancer.gov/dhq2/dietcalc/>).

Dietary Glycemic Measures

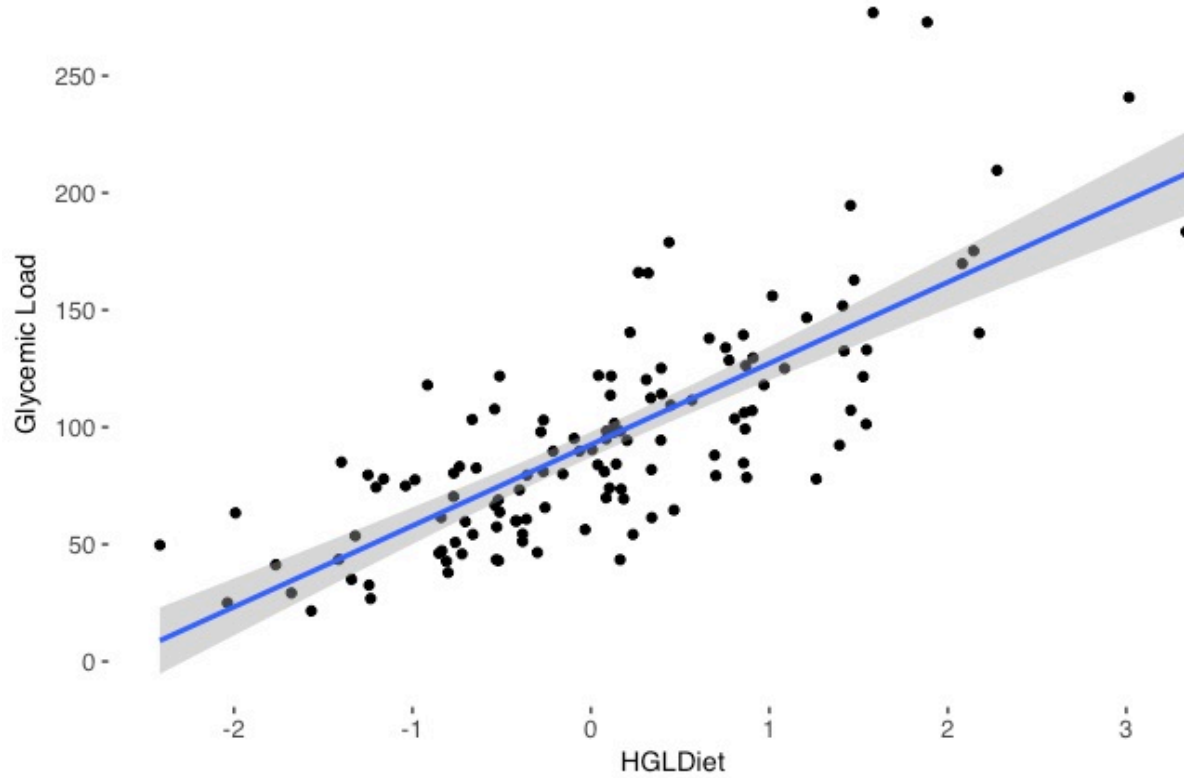
We examined four dietary glycemic measures derived from the DHQII: daily intake of carbohydrate, sugar, glycemic load and adherence to a high glycemic load diet pattern. Three of these measures represent output variables from the DHQII (daily intake of carbohydrate, sugar and glycemic load) while adherence to a high glycemic load diet pattern was determined using principal components analysis (PCA).

PCA was used to identify adherence to a glycemic load dietary pattern. Food variables were established using *My Pyramid Equivalents Database 2.0* (MPED 2.0) (130) which includes 32 food groups derived from 7,752 different foods. All food variables were entered into the factor analysis and rotated with the varimax rotation method to maximize interpretability of the data. Factor loading scores were computed for each individual food group. Higher factor loading values represent stronger correlations between each individual food group and its contribution to a specific dietary pattern. The first rotated factor from the PCA, which explained 13.7% of the total data variance, exhibited high loading factors on food groups that are associated with high glycemic load; it was, therefore, labeled the High Glycemic Load Diet pattern (HGLDiet pattern). Individual factor regression scores, which represent a quantitative value of individual adherence to a specific dietary pattern, were calculated for each study participant by summing the intake of each food group multiplied by its factor loading

value from the HGLDiet pattern component. Linear regression was used to evaluate the association between the HGLDiet pattern factor scores and daily glycemic load scores. The HGLDiet pattern was strongly correlated with daily glycemic load ($r^2=0.58$, $p < 0.001$, Figure 1) and daily sugar intake ($r^2=0.27$, $p < 0.001$), which rationalized the designation of this dietary pattern.

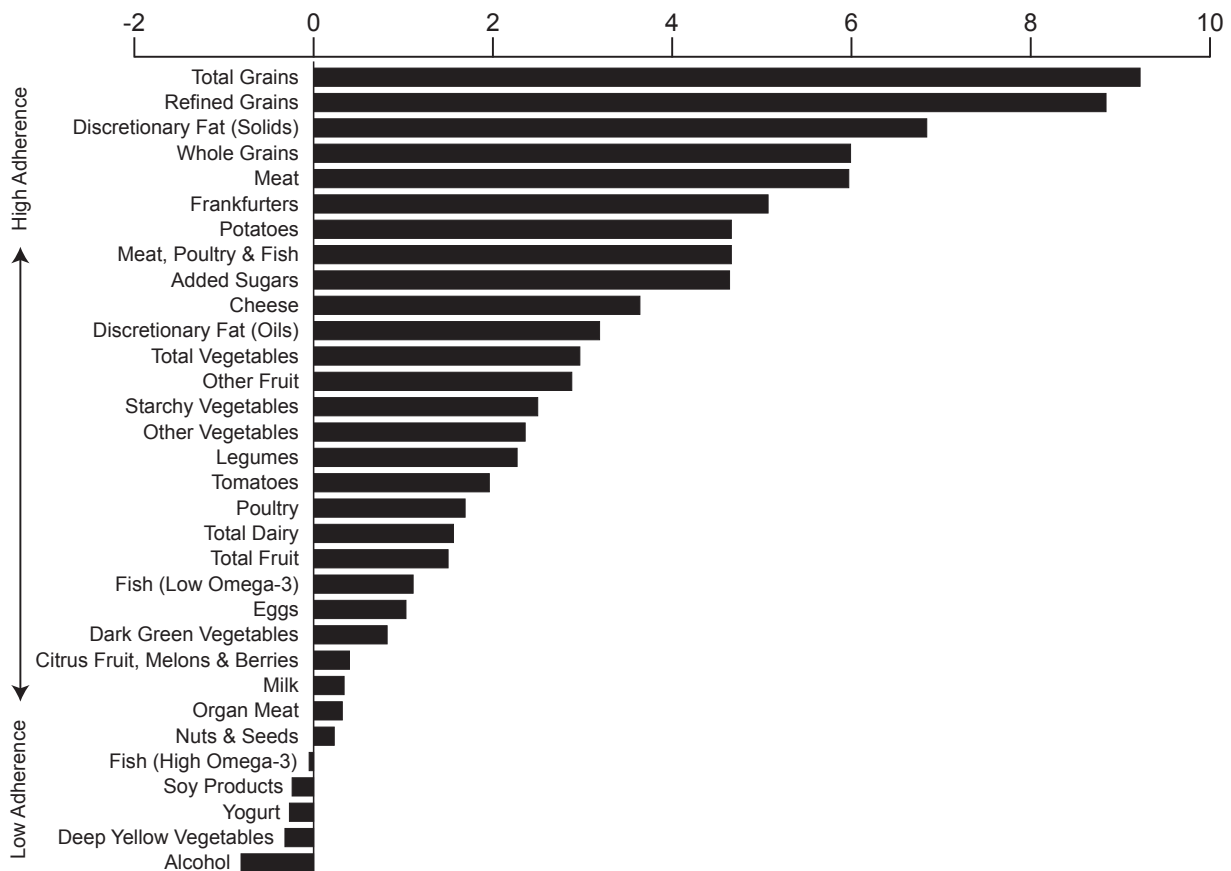
Rotated factor loadings for the individual food groups and the HGLDiet pattern are shown in Figure 2. The HGLDiet pattern was characterized by high intake of high glycemic load foods such as total grains, refined grains, potatoes, starchy vegetables and added sugars. Whole grains, lean and fatty meat and discretionary fats also loaded positively on this dietary pattern.

Figure 1 The relationship between Glycemic Load and HGLDiet pattern



The HGLDiet pattern was highly correlated with glycemic load intake ($r^2=0.58$, $p < 0.001$) thus justifying the name of this diet pattern

Figure 2 Rotated factor loadings for the High Glycemic Load Diet pattern



Factor loading coefficients are represented as the bars (10x). Greater intake of foods that have high positive loading coefficients results in higher HGLDiet pattern adherence scores. Greater intake of foods with low or negative loading coefficients results in low/negative HGLDiet pattern adherence scores.

Anthropometric assessment

Body weight and height were measured for all subjects. Body weight was measured with a calibrated scale (± 0.1 kg). Height was measured with a wall-mounted stadiometer. BMI (kg/m^2) was calculated using weight and height measurements.

Assessment of Cerebral Amyloid Burden

PET images were obtained on a GE Discovery ST-16 PET/CT scanner after administration of intravenous florbetapir F-18 (370 MBq). Two PET brain frames of five minutes in duration were acquired continuously approximately 50 minutes post-injection. Frames were then summed and attenuation corrected prior to interpretation. MIMneuro software (MiM Software Inc, Cleveland, OH) quantitatively normalized the amyloid- β PET image to the entire cerebellum to calculate the Standard Uptake Value Ratio (SUVR) for six regions of interest (ROIs): anterior cingulate, posterior cingulate, precuneus, inferior medial frontal, lateral temporal and superior parietal cortex using a proprietary algorithm. The mean of these 6 ROIs was calculated as the global SUVR. Three trained raters reviewed the visual images, the quantitative SUVR ROI data and MIMneuro-generated cortical projections of amyloid burden (z-scores comparing the SUVRs to an SUVR map of 74 individuals (48 males, 26 females) between the ages of 18-50) to assess the scans as “elevated” or “non-elevated”. The final determination of elevated or non-elevated was determined by majority (i.e., ≥ 2 raters in agreement).

Neuropsychological Testing

All participants completed a standard battery of neuropsychological tests that included the Mini-Mental State Exam (MMSE), the Wechsler Adult Intelligence Scale – Revised (WAIS-R) Digit Symbol, Trail Making Test A, Trail Making Test B, Category Fluency (animals and vegetables), the Stroop Color-Word Interference Test, the WAIS-R Block Design and the total free recall score from the Free and Cued Selective Recall Test (126). Each neuropsychometric test score was converted to a z-score by

subtracting the study population mean from each individual test score and dividing by the study population standard deviation. Higher scores on the Trail Making Test A and Trail Making Test B indicate greater cognition impairment, thus z-scores for these tests were multiplied by -1 so that negative scores reflect greater impairment of cognition. A global cognition z-score was established by calculating the mean of the combined cognitive z-scores.

Statistical Analyses

The primary focus of this study was to investigate the relationship between regional and global cerebral amyloid burden (SUVR) and dietary glycemic measures: HGLDiet pattern adherence, carbohydrate intake, sugar intake and glycemic load. All continuous variables were expressed as mean daily intake \pm SD. Differences between the elevated and non-elevated groups were assessed using one-way ANCOVA. Linear regression models were used to investigate the relationships between the continuous variables with regional cerebral amyloid burden (SUVR). For all dependent variables, residual analyses were performed to assess applicability of linear regression and normality was assessed using the Shapiro-Wilk test for normality. Residual normality issues were discovered, thus, we identified outliers using a modified z-score method (134) removing cases above a threshold of 3.5. Two cases were excluded due to very high SUVR values which resolved residual normality issues without affecting statistical conclusions. Dependent data with non-normally distributed residuals were log transformed. All analyses were controlled for age and gender. Cognitive analyses were further controlled by education level and analysis of relationships between dietary

components and cerebral amyloid burden were further controlled by education level and BMI. Energy intake and oral diabetes medications were considered as regression covariates but had no effect on statistical outcomes. Statistical analyses were performed using R (v. 3.3.1; R Foundation, Vienna, Austria). Statistical significance was set at $p < 0.05$.

RESULTS

Data from 126 cognitively normal participants ranging in age from 65-90 years (71.6 ± 5.2 years) were included. Amyloid scans were interpreted as elevated in 25.4% ($n=32$) of the participants, in line with the expected prevalence of elevated cerebral amyloid in cognitively normal older adults (135). Amyloid burden, anthropometric, neuropsychometric, dietary intake and cerebral amyloid characteristics are presented in Table 1.

We first examined whether there were differences in dietary glycemic measures across amyloid elevated and non-elevated groups (Table 3). Controlling for age and gender, the elevated amyloid group had significantly higher adherence to the HGLDiet pattern ($p=0.015$) compared to the non-elevated group with a trend for higher daily sugar intake in those with elevated amyloid ($p=0.065$). There were no differences across amyloid groups for daily carbohydrate intake and daily glycemic load.

Table 3 Participant Characteristics

	Overall (n=126)	Elevated (n=32)	Non-elevated (n=94)	p-value
Age, y	71.3 ± 5.1	72.5 ± 4.6	71.0 ± 5.2	0.148
Gender (Female/Male)	83/43	19/13	64/30	0.495
% Female / % Male	66% / 34%	59% / 41%	68% / 32%	-
BMI, kg/m ²	28.9 ± 4.8	28.4 ± 4.2	29.0 ± 5.0	0.507
Diagnosed Diabetes	16 (12.7%)	6 (18.8%)	10 (10.6%)	0.377
Taking Oral DM Meds	15 (11.9%)	5 (15.6%)	10 (10.6%)	0.663
Education (years)	16.5 ± 2.6	16.4 ± 3.1	16.6 ± 2.4	0.780
Dietary Intake¹				
Energy, kcal	1584.7 ± 673.4	1697.7 ± 757.8	1546.5 ± 642.1	0.352
Fat, g	65.5 ± 31.1	68.0 ± 31.1	64.7 ± 31.2	0.669
Protein, g	65.1 ± 32.0	68.6 ± 29.0	63.9 ± 33.1	0.561
Dietary Glycemic Measures¹				
Carbohydrate, g	184.4 ± 84.7	207.8 ± 111.8	176.4 ± 72.3	0.106
Sugar, g	86.1 ± 49.2	101.6 ± 64.1	80.8 ± 42.0	0.065
Glycemic Load	95.5 ± 47.0	106.0 ± 57.5	92.0 ± 42.6	0.202
HGLDiet Pattern	0.09 ± 1.03	0.48 ± 1.1	-0.05 ± 1.0	0.015*
Cognition Scores				
MMSE	29.0 ± 1.4	29.0 ± 1.0	28.9 ± 1.5	0.937
WAIS – R Digit Symbol	50.7 ± 10.0	48.7 ± 9.5	51.4 ± 10.2	0.179
Trail Making Test A	29.1 ± 9.7	30.7 ± 9.5	28.6 ± 9.8	0.301
Trail Making Test B	78.6 ± 37.5	77.7 ± 25.0	78.9 ± 41.1	0.878
Category Fluency	38.9 ± 8.3	38.2 ± 7.9	39.2 ± 8.4	0.542
Block Design	36.6 ± 10.8	35.3 ± 9.9	37.1 ± 11.1	0.410
Stroop	219.1 ± 31.6	215.5 ± 31.9	220.4 ± 31.6	0.453
SRT – Free Total	30.6 ± 5.2	29.0 ± 5.3	31.1 ± 5.0	0.050*
SUV²				
Global	1.07 ± 0.16	1.29 ± 0.16	0.99 ± 0.06	<0.001*
Anterior Cingulate Gyrus	1.15 ± 0.20	1.42 ± 0.20	1.05 ± 0.08	<0.001*
Inferior Medial Frontal Gyrus	1.00 ± 0.17	1.24 ± 0.17	0.92 ± 0.06	<0.001*
Lateral Temporal Lobe	1.09 ± 0.16	1.29 ± 0.17	1.02 ± 0.08	<0.001*
Posterior Cingulate Gyrus	1.05 ± 0.15	1.23 ± 0.16	0.99 ± 0.08	<0.001*
Precuneus	1.11 ± 0.21	1.39 ± 0.22	1.02 ± 0.08	<0.001*
Superior Parietal Lobule	1.01 ± 0.15	1.18 ± 0.16	0.95 ± 0.09	<0.001*

Abbreviations: BMI, body mass index; HGLDiet Pattern, High Glycemic Load Diet pattern; MMSE, Mini-Mental State Exam; WAIS – R, Wechsler Adult Intelligence Scale – Revised; Stroop, Stroop Color-Word Interference Test; SRT, Selective Reminding Test; SUV², standard uptake value ratio

Values are mean ± standard deviation

Adjusted for Age and Gender

¹Derived from food frequency questionnaire

²Derived by florbetapir F-18 PET imaging

*Significant difference between groups (p ≤ 0.05)

We next examined the relationship of dietary glycemic measures with regional and global measures of cerebral amyloid burden (SUVR) in the overall group using linear regression controlling for age, gender, education level and BMI. All four measures of glycemic intake were positively associated with global and regional measures of cerebral amyloid load (Table 4). Figure 3 demonstrates the relationship of adherence to the HGLDiet pattern with global cerebral amyloid levels. Figure 4 illustrates the relationship between the HGLDiet pattern and regional cerebral amyloid using voxel-based morphometry regression analyses.

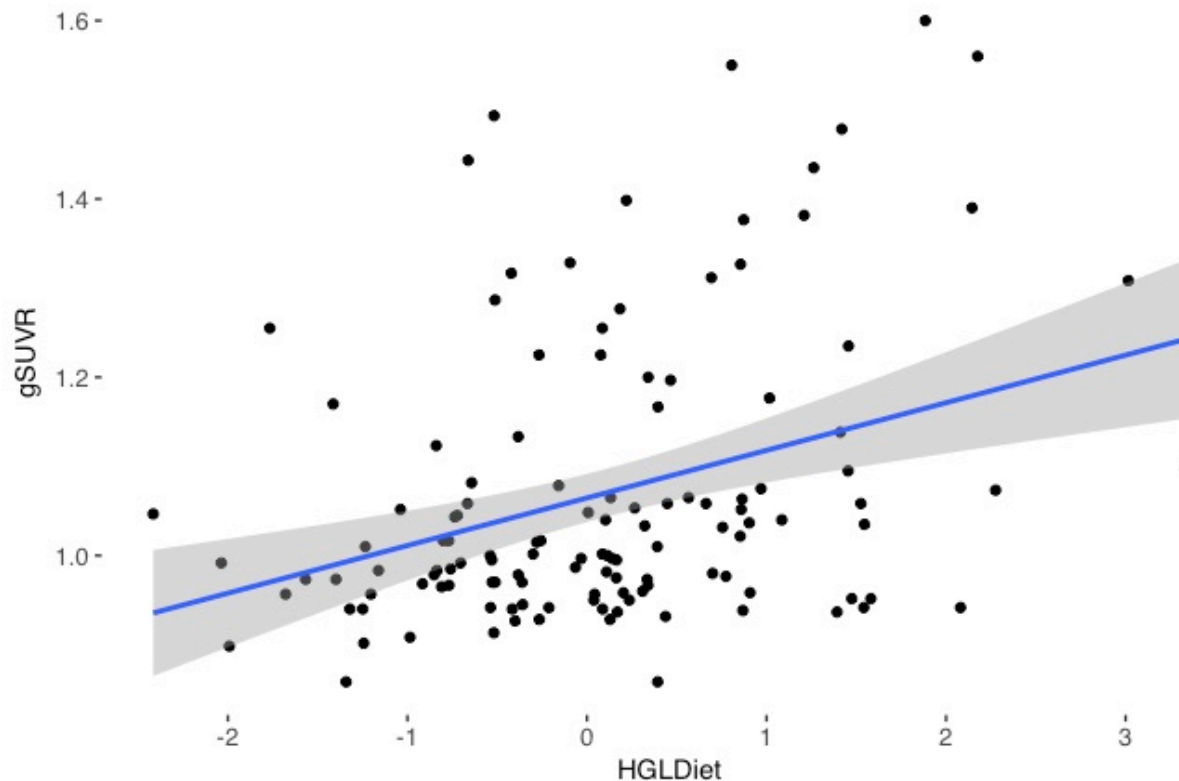
Table 4 Relationship of glycemic dietary intake measures with global and regional cerebral amyloid burden.

	HGLDiet Pattern	Sugar Intake	Glycemic Load	Carbohydrate Intake
Global	0.36***	0.21*	0.22*	0.24*
Anterior Cingulate Gyrus	0.38***	0.20*	0.23*	0.25**
Inferior Medial Frontal Gyrus	0.33***	0.17	0.16	0.18
Lateral Temporal Lobe	0.34***	0.22*	0.22*	0.24*
Posterior Cingulate Gyrus	0.31***	0.17	0.18*	0.21*
Precuneus	0.32***	0.22*	0.21*	0.24*
Superior Parietal Lobule	0.30***	0.19*	0.20*	0.21*

Values are the estimated standard deviation change in cerebral amyloid burden (SUVR) per 1 standard deviation change in the respective dietary glycemic measure (standardized coefficients) after controlling for age, gender, education level and BMI.

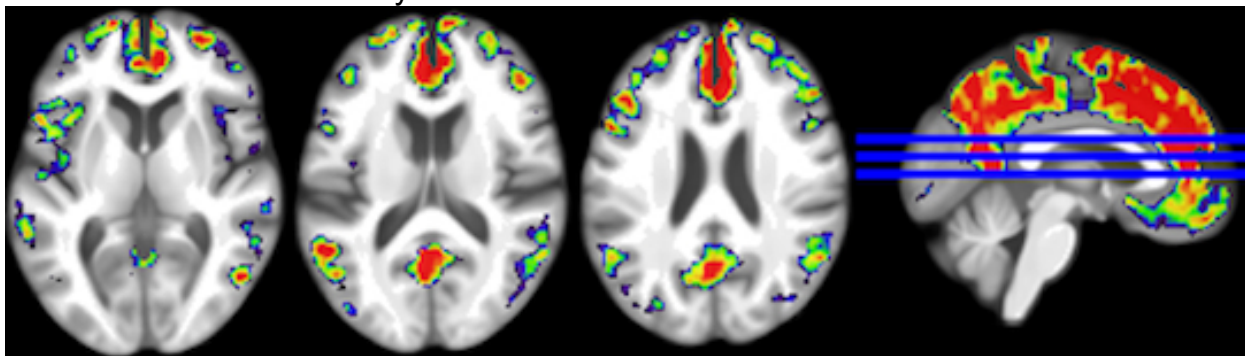
* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$

Figure 3 Association of High Glycemic Load Diet pattern adherence with global cerebral amyloid burden.



The correlation of HGLDiet pattern adherence scores with global amyloid burden. HGLDiet pattern adherence explained 12% of the variability in global cerebral amyloid burden ($r^2=0.12$, $p \leq 0.001$). HGLDiet pattern adherence was also significantly correlated with amyloid burden in all regions of interest.

Figure 4 Visualization of the relationship between High Glycemic Load Diet pattern adherence and cerebral amyloid burden.



The High Glycemic Load Diet pattern (HGLDiet pattern) measure was regressed against Standardized Uptake Value Ratios for all participants. Standardized beta values are projected on the MNI152 anatomical template, with warmer colors representing regions of greater association with HGLD.

We also examined how dietary glycemic measures related to cognitive performance. Cognitive analyses were controlled for age, gender and education level. Daily sugar intake negatively correlated with global cognition and cognitive performance on several individual neuropsychometric tests (Table 5) including MMSE, Trail Making Test B, WAIS-R Digit Symbol, and Block Design. No other dietary measures exhibited relationships with neuropsychometric test scores.

Table 5 Relationship of glycemic dietary intake measures with cognitive performance.

	HGLDiet Pattern	Sugar Intake	Glycemic Load	Carbohydrate Intake
Global	-0.01	-0.26**	-0.15	-0.16
MMSE	-0.07	-0.18*	-0.16	-0.11
WAIS-R Digit Symbol	0.07	-0.23*	-0.13	-0.13
Trail Making Test A ¹	0.02	-0.15	-0.07	-0.08
Trail Making Test B ¹	0.02	-0.29**	-0.16	-0.17
Category Fluency	-0.11	-0.17	-0.15	-0.15
Stroop	0.05	-0.01	0.04	0.03
Block Design	0.06	-0.20*	-0.11	-0.13
SRT – Free	-0.04	-0.15	-0.06	-0.12

Abbreviations: MMSE, Mini-Mental State Exam; WAIS – R, Wechsler Adult Intelligence Scale – Revised; Stroop, Stroop Color-Word Interference Test; SRT, Selective Reminding Test

Values are the estimated standard deviation change in cognitive performance per 1 standard deviation change in the respective dietary glycemic measure (standardized coefficients) after controlling for age, gender and education level.

¹For consistency with other measures, we multiplied z-scores for Trail Making Test A and B so that negative scores reflect cognitive decline

*p ≤ 0.05, **p ≤ 0.01, ***p ≤ 0.001

DISCUSSION

The current study provides evidence that a high glycemic diet is associated with increased global and regional cerebral amyloid burden in cognitively normal older adults. We estimated 4 different dietary glycemic measures derived from the DHQII food

frequency questionnaire – daily intake of sugar, carbohydrate, glycemic load and adherence to a PCA-derived dietary pattern characterized by intake of highly glycemic foods – and found strong relationships with cerebral amyloid load for each measure. A modest negative association was found between sugar intake and cognitive performance but no other dietary glycemic measures. These data suggest that diet may be a modifiable risk factor that may influence cerebral amyloid deposition, providing additional evidence linking glucose metabolism with AD pathophysiology.

Our data add to the growing body of evidence linking glucose metabolism with chronic disease. For instance, high carbohydrate intake and glycemic load have been linked with increased risk of insulin resistance, type 2 diabetes, coronary artery disease, stroke, and multiple cancers (96, 136, 137). Our data extend this evidence by linking dietary glycemic measures directly with a primary AD biomarker in cognitively normal older adults. Individuals with cerebral amyloid plaques in the absence of cognitive symptoms are at higher risk of cognitive decline (138-140), brain atrophy (69, 141), and progression to AD (142), although not all amyloid-positive individuals will develop dementia. Currently, precise estimates of the magnitude and timeframe for future risk of dementia are not available on an individual basis although imaging and pathological studies suggest plaques may accumulate up to 10 to 15 years prior to the onset of clinically recognized dementia (143).

To date only limited data address the relationship between nutrition and cerebral amyloid. A prior longitudinal imaging initiative demonstrated that nutrient intake patterns related to vitamin B12, vitamin D, zinc, and omega 3 fatty acid consumption associated with less amyloid deposition (65, 66). Another study found an inverse relationship

between serum docosahexanoic acid (DHA), an omega-3 fatty acid found abundantly in fatty fish, and cerebral amyloid burden in older adults with normal cognition and MCI (68). In addition to these amyloid findings, higher intake of sugary beverages is associated with decreased brain volume and poorer episodic memory performance (144). We believe our study extends these observations by being the first to link amyloid deposition with dietary glycemic measures. Our finding that a high glycemic diet associates with with greater amyloid deposition is consistent with our prior work on a subset of the current cohort that found impaired fasting glycemia associates with increased amyloid burden in highly metabolic regions of the brain in cognitively normal older adults (67).

It is well established that diets with greater intake of sugar, high glycemic index foods, and overall carbohydrate are linked to impaired glucose metabolism, including insulin resistance and type 2 diabetes (96), both risk factors for AD and cognitive decline (71, 72). Emerging evidence indicates that glucose and insulin status may influence the modulation of cerebral amyloid accumulation (80) and that elevated glucose may evoke a state of decreased metabolism in the brain (76-79). Protein homeostasis requires a steady flux of energy; bioenergetic perturbations that arise due to elevated glycemia and insulin resistance may potentially contribute to altered amyloid precursor protein or beta amyloid processing (8). Relevant to this point, an AD mouse model study in which acute hyperglycemia was induced through the intravenous flow of dextrose increased amyloid levels in the brain interstitial fluid compartment (81). Acute hyperglycemia from the consumption of processed carbohydrates and sugars could potentially mimic this effect.

To further validate our findings, we also looked for possible relationships between dietary glycemic measures and cognitive performance. While 3 of the dietary glycemic measures did not associate with cognitive performance, higher sugar intake was found to inversely correlate with global cognitive performance (as measured by a global composite measure and the MMSE) and with individual tests in our battery (Digit Symbol, Trailmaking B and Block Design). Prior studies have demonstrated detrimental cognitive effects of high sugar and high glycemic index feedings in human and animal studies. Adults with type 2 diabetes fed a meal of high glycemic index/high sugar foods exhibited poorer acute cognitive performance (145) and cognition changes have also been observed in rats fed high sucrose and high-fructose corn syrup diets (98, 99, 146). While cognitive changes are believed to be induced by poor glycemic control, it is unclear as to why cognitive performance in this study was only related to sugar intake and not other dietary glycemic measures.

Our study has several strengths. It featured a sample size of over 125 well-screened, cognitively normal older adults that underwent amyloid PET imaging. The inclusion of only underactive or sedentary individuals controlled for any potential differences in physical activity and is relevant considering the majority of older adults are sedentary more than 8.5 hours of the day (147). An additional strength of this study was the input of MPED 2.0 variables into PCA analysis to identify and characterize the HGLDiet pattern. MPED 2.0 translates dietary intake into quantitative food group variables, effectively reducing the number of dietary variables to consider for analysis and collinearity of foods with their corresponding nutrients. Using PCA in this study allowed us to identify dietary patterns existing within the data collected, describe

interpersonal dietary intake differences and conduct a more comprehensive analysis of dietary intake than solely that of solitary nutrients (148). Finally, showing a modifiable behavior, diet, influences an AD biomarker could have strong preclinical applications.

There were also limitations that should be considered. Cross-sectional studies are not designed to establish causal relationships. Food frequency questionnaires are demonstrated to be accurate yet are potentially subject to underreport or over report of some nutrients by individuals. The DHQII estimates dietary intake over the past year, leaving some question of chronic intake over the course of the subjects' lifetime. Additionally, it is possible that amyloid status, converse to our interpretation, influences dietary intake.

In conclusion, future studies are needed to further investigate the impact of carbohydrate intake on cerebral amyloid processing. Nevertheless, these findings in cognitively normal older adults suggest that dietary intake may influence amyloid accumulation prior to AD symptomology. Although the clinical relevance of amyloid burden in older adults is not precisely defined, the presence of brain amyloid aggregations does imply an elevated risk of future symptomatic dementia. Understanding the mechanisms through which dietary intake influences brain health and beta amyloid accumulation could have public health implications and suggest potential lifestyle-based AD prevention strategies.

**Chapter Four: Feasibility and Efficacy of a Medium Chain Triglyceride
Supplemented Ketogenic Diet in Alzheimer's**

Abstract

Background: Cerebral glucose metabolism is reduced in patients with Alzheimer's disease (AD). An alternative substrate, ketones, crosses the blood brain barrier and can be utilized for brain metabolism. It is unknown whether the ketogenic diet (high fat, low carbohydrate) is feasible or beneficial for patients with AD. The objective of this study was to assess feasibility of a 3-month medium chain triglyceride supplemented ketogenic diet (MCT-KD) in AD patients and generate preliminary efficacy data.

Methods: Fifteen participants with a diagnosis of Alzheimer's disease were recruited to a single-arm clinical trial where they consumed the MCT-KD for 3 months. At month 3, participants terminated the MCT-KD and resumed a normal diet for a 1-month washout period. Ketone generation was monitored through daily checking of urinary ketone status by the participant and monthly serum β -hydroxybutyrate assessment. Dietary intake was collected through baseline and monthly 3-day food records. Cognition was measured through administration of the mini mental state exam and the Alzheimer's Disease Assessment Scale-cognitive subscale at baseline, after 3 months of the dietary intervention and after the 1-month washout period.

Results: The MCT-KD was feasible in individuals with AD as 10 of the 15 participants produced urinary and serum ketones during the 3-month intervention. Urinary acetoacetate was detected an average of 54.5 days (60.6%) of the intervention in study completers. Serum β -hydroxybutyrate was significantly elevated from baseline at all 3 monthly time points during the diet intervention ($p \leq 0.001$ for each). Improvements in ADAS-cog scores were observed from baseline to month 3 (4.1-point mean improvement, $p=0.02$) and improvements diminished after the 1-month washout.

Conclusion: Data from this pilot study demonstrated that a 3-month MCT-KD is feasible in patients with AD (CDR 0.5 and CDR 1) and may elicit positive changes in cognition.

INTRODUCTION

It is estimated that cerebral metabolism accounts for 20% or greater of total body metabolism, thus the brain requires a substantial supply of energy (28, 29). Energetic demands of the brain are typically met by circulating glucose derived from carbohydrates consumed in the diet, which are quite plentiful in the common Western diet (30). Individuals with Alzheimer's disease have consistently demonstrated reductions in cerebral glucose utilization, potentially reaching regional deficit of up to 33% when compared to age matched adults with normal cognition (26, 34, 35). Alternatively, when available, the brain uses a secondary energy substrate, ketones (33). Ketone metabolism in AD remains unaffected and could potentially compensate for glucose metabolism deficit (121, 149).

Ketones result from the mobilization of fatty acids to the liver where they undergo conversion from fatty acids to ketones. There are three common manners in which serum ketone levels are elevated, 1) through increased mobilization of endogenous fatty acids due to prolonged fasting (103), 2) through adherence to a ketogenic diet (KD) characterized by fat intake greater than 70% of total energy and reduction of carbohydrate to approximately 5% of total energy (104), and 3) through intake of ketogenic agents, such as medium-chain triglycerides (MCT), or exogenous ketone substrates (105, 106).

Therapeutic use of the KD in intractable infantile epilepsy is well studied and has been extensively applied clinically (150). KD proposal as a potential therapy in AD is not novel, however, clinical data are sparse (119, 151, 152). AD patients that consumed an MCT, caprylic triglyceride, for 90 days demonstrated elevated beta-hydroxybutyrate

(BHB) levels 4-fold by day 90 and had better Alzheimer's Disease Assessment Scale-Cognition Subtest (ADASCog) scores than the placebo group (105). Patients diagnosed with Mild Cognitive Impairment (MCI) randomized to restriction of carbohydrate as 5-10% of total energy intake for 6 weeks exhibited elevated urine ketones and improved verbal memory scores while no changes were observed in those assigned to the high carbohydrate arm of the study (123). Furthermore, feeding of a ketogenic meal to non-demented elderly positively affected working memory, visual attention, and task switching (153).

The primary aim of the current study was to determine the feasibility of an MCT-supplemented KD in varying levels of AD. Our secondary aim was to evaluate cognitive outcomes associated with following the ketogenic diet.

METHODS

Study Design

In this single-arm pilot clinical study, patients were recruited to follow the MCT-KD for 3 months. Immediately upon completion of the 3-month dietary intervention, participants were asked to discontinue the MCT-KD and resume a normal diet for the 1-month washout period.

Participants

Fifteen older adults with cognition impairment were enrolled in the Ketogenic Diet Retention and Feasibility Trial (KDRAFT). Participants were recruited through the University of Kansas Alzheimer's Disease Center. Individuals were eligible to participate

in the study if they had a clinical dementia rating (CDR) (125) of very mild AD, CDR 0.5; mild AD, CDR 1; or moderate AD, CDR 2, had an active study partner, BMI ≥ 21 kg/m², normal electrolytes and liver function and spoke English. Exclusion criteria included serious medical risk including type 1 diabetes, ongoing or recent cancer, cardiac event in the past year or other conditions deemed serious risks by physicians on the study team. The study protocol was approved by the Institutional Review Board at the University of Kansas Medical Center. Informed consent was obtained from all study participants per institutional guidelines.

MCT-KD Intervention

All participants were assigned to the 3-month MCT-KD dietary intervention. Participants received nutrition counseling for the MCT-KD from the study dietitian at the baseline study visit. Target macronutrient composition for the dietary intervention included approximately 70% of energy as fat, 20% of energy as protein and restriction of carbohydrate to less than 10% of energy; a ketogenic ratio of 1:1 (ratio of energy from lipid to energy from non-lipid) or better. Energy intake requirement and target daily MCT dosage was estimated using the Mifflin-St. Jeor equation (154). A monthly supply of MCT oil (Now Foods, USA) was provided at each study visit. MCT dosage titrated from 10% of total energy from fat in the first week, increasing by 10% of total energy from fat for the subsequent weeks until reaching a target dose of 40% of total energy from fat. Participants reached target dosage, but titration rate was adjusted based upon participant tolerance. Daily multivitamin, vitamin D, calcium and phosphorus supplements were provided to prevent potential micronutrient deficiency. Upon

completion of the MCT-KD, participants were instructed to discontinue the MCT-KD to complete a 1-month washout period.

Dietary Intake

Three-day food records (3DFR) were collected at baseline, month 1, month 2 and month 3 to characterize dietary intake before, during and after the dietary intervention. Each 3DFR recorded intake for 2 weekdays and 1 weekend day. At the baseline visit, the study dietitian provided instruction for 3DFR completion. Food record data were entered into the Nutrition Data System for Research (NDSR; v. 2016) to analyze nutrient intake.

Urinary Ketones

Participants self-monitored urinary ketones daily in the early evening using urinary acetoacetate test strips (Ketostix, Bayer, Germany). Daily urinary ketone status was recorded as either negative, trace, small, moderate or large in a provided diary. Days in which participants did not measure ketone levels were conservatively tallied as a “negative” ketone response.

Serum Biomarkers

All serum biomarkers were collected after a 12 hour fast. A full lipid and metabolic panel were collected at baseline and month 3 (end of diet intervention) and measured by commercially available kits. Serum BHB and insulin levels were measured at all clinical visit time points (baseline, month 1, month 2, month 3 and washout) and

quantified using commercially available kits. HOMA2-IR was calculated using HOMA2 Calculator (v. 2.2.3; University of Oxford, United Kingdom). Blood draws were performed by the KU Clinical Translational Science Unit nursing staff and results were processed by the KU Hospital Clinical Laboratories.

Cognitive Testing

Secondary outcomes included measures of cognition. A trained psychometrician administered the Mini-Mental State Exam (MMSE) and the Alzheimer's Disease Assessment Scale Cognitive Subscale (ADAS-cog) at baseline, end of intervention (month 3) and after the 1-month washout. The MMSE is a brief, 30-point questionnaire designed to identify cognitive impairment (128). The ADAS-cog consists of 11 tasks that measure changes in memory, language, praxis and attention (155). Total incorrect answers and cued reminders are reported as the cumulative score, thus higher scores on the ADAS-cog reflect greater cognitive impairment.

Anthropometric Measures

Height, weight and body composition were measured for all subjects by trained CTSU staff. Body weight was measured with a calibrated scale (± 0.1 kg). Height was measured with a wall-mounted stadiometer. BMI (kg/m^2) was calculated using weight and height measurements. Dual energy x-ray absorptiometry (DEXA) was used to attain and quantify body fat percentage, lean body mass, fat mass and bone mass at baseline and month 3.

Statistical Analyses

Continuous variables were described using their means and standard deviations (SD). Descriptive statistics were utilized to quantify and characterize feasibility of the intervention. Normality of the dependent variables was assessed through Q-Q visualization of residuals models. Paired t-tests were used to analyze differences in dietary macronutrient intake prior to and during diet intervention. We constructed linear mixed models and tested mean differences with post-hoc pairwise comparisons for cognitive data, parametric serum biomarkers. Friedman tests with Conover post-hoc pairwise comparisons were performed on serum beta-hydroxybutyrate data. Statistical analyses were performed using R (v. 3.3.2; R Foundation, Vienna, Austria). Statistical tests were two-tailed and significance was set at $p < 0.05$.

RESULTS

Participants

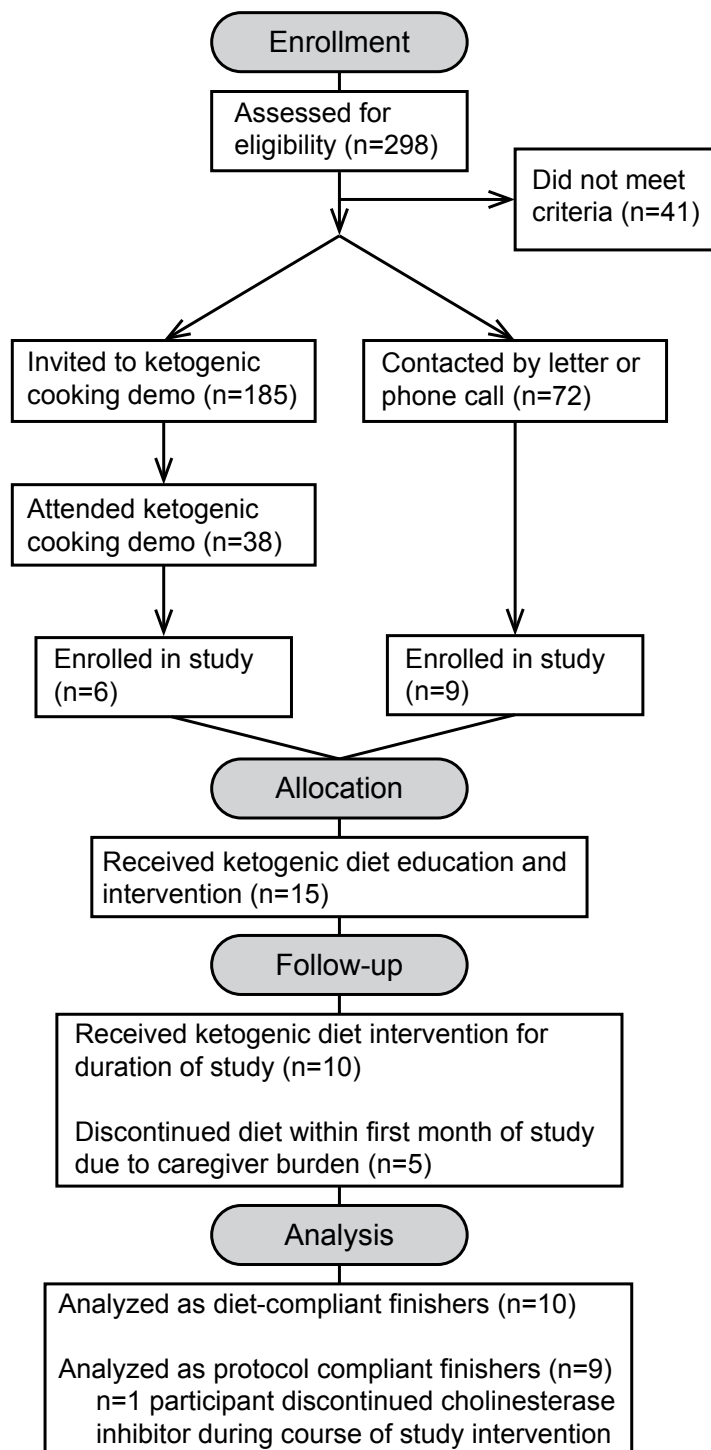
Fifteen participants meeting the McKhann et al. criteria for AD (156) enrolled in the study over the course of 31 months (December 2013-July 2016). Refer to Table 6 for demographics. 298 individuals with a diagnosis of AD were screened for the study. For the first year and 7 months of the enrollment period, potential participants were individually identified and screened then contacted by the study coordinator by either letter or phone call. Of 72 potential participants contacted, 9 participants enrolled in the study. We invited 185 participants by letter to ketogenic cooking demos that were offered on 2 different dates. Thirty-eight total potential participants attended 1 of the 2 cooking demonstrations at the KU Clinical Research Center Demonstration Kitchen,

resulting in the enrollment of 6 new participants. Figure 5 depicts the CONSORT (<http://www.consort-statement.org>) profile.

Table 6 Participant Characteristics (n=15)

	Mean (SD)
Age, y	73.1 (9.0)
Gender (Male/Female)	7 / 8
BMI, kg/m ²	28.3 (6.8)
Education	15.0 (2.7)
Clinical Dementia Rating	
CDR 0.5	7
CDR 1	4
CDR 2	4

Figure 5 CONSORT diagram demonstrating study profile and course.



Feasibility

Of the participants enrolled in the study, 5 participants did not successfully implement the MCT-KD and withdrew from the study within the first month (dropout rate of 33%) and provided only baseline data. Four of the dropouts had a diagnosis of moderate AD (CDR 2) and the other had a diagnosis of very mild AD (CDR 0.5). Table 7 summarized the course of the diet and cognitive outcome for each subject. All study partners of the participants that withdrew early cited caregiver burden as reason for withdrawal from the study. The remaining 10 participants were compliant with the MCT-KD, however, one participant was considered protocol non-compliant having discontinued the cholinesterase inhibitor prescribed for AD symptoms. This was the only participant to experience cognitive decline.

Table 7 Individual course of diet

Subject ID	CDR	Data for Analysis	ADAS-cog ¹	Time/Reason for Dropout
01	0.5	X	Improve	Week 2/Caregiver Burden
02	0.5			
05	0.5	X	Decline	
06	0.5	X	Improve	
07	0.5	X	Improve	
11	0.5	X	Improve	
13	0.5	X	Improve	
08	1	X	Improve	
10	1	X	Improve	
14	1	X	Improve	
15	1	X	No change	
03	2			Week 4/Caregiver Burden
04	2			Week 4/Caregiver Burden
09	2			Week 5/Caregiver Burden
12	2			Week 4/Caregiver Burden

Abbreviations: CDR, clinical dementia rating; ADAS-cog, Alzheimer's Disease Assessment Scale cognitive subscale

The table demonstrates the participants that completed the 3-month dietary intervention as well as individual reasons for dropout and time point.

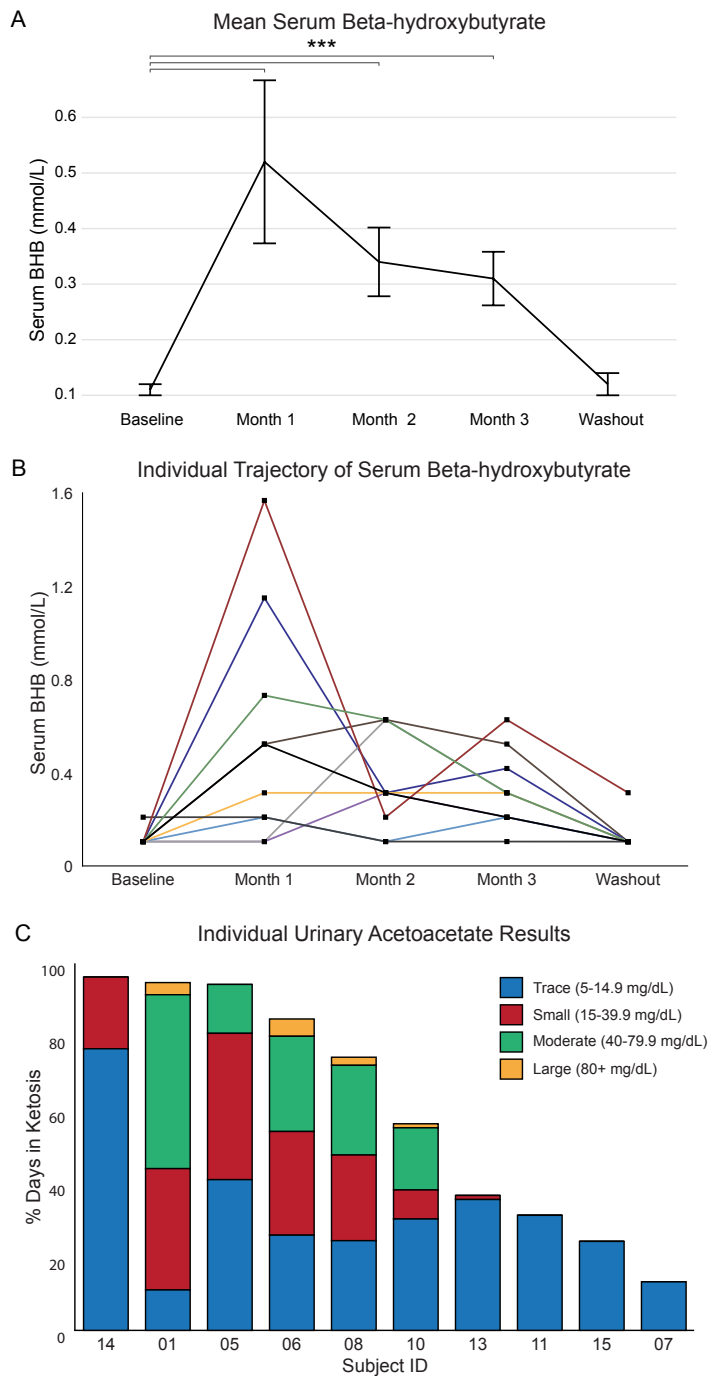
¹ADAS-cog changes from baseline to month 3.

Ten study finishers achieved urinary ketones through the course of the 3-month intervention. Self-reported records indicated that finishers attained ketosis an average of 54.5 ± 29.0 (60.6%) days of the 3-month dietary intervention. Ketones were detected as trace (5-14.9 mg/dL)=49%, small (15-39.9 mg/dL)=26%, moderate (40-79.9 mg/dL)=23% and large (80+ mg/dL)=2% of the total days spent in ketosis. Urinary ketone responses were reflected well by serum BHB results with one exception. One participant recorded urinary ketones 24.2% only reached trace levels while their serum BHB levels were considerably elevated at each study visit. Urinary ketone results are presented in Figure 6.

Serum BHB was significantly elevated at months 1, 2 and 3 from baseline (0.11 mmol/L, 0.52 mmol/L, 0.34 mmol/L, 0.31 mmol/L; $p < 0.001$ for each). Serum BHB returned to normal at the end of the washout period. Mean and individual BHB values are presented in Figure 6.

Table 8 contains all values for anthropometric measures, serum biomarkers, metabolic measures and dietary intake.

Figure 6 Participant ketone measures



A) Mean serum ketone levels at all time points. Serum ketones were significantly elevated from baseline at months 1, 2 and 3 (the duration of the MCT-KD intervention). B) The individual serum ketone trajectory for all time points. Serum ketone levels returned to normal after the 1-month washout period. C) The individual urinary ketone results from daily testing. Ketones were detected an average of 54.5 ± 29.0 days. The majority of results were trace or small ketones, while some participants recorded moderate and large ketone results.

*** $p \leq 0.001$

There was no difference in energy intake prior to implementation of versus during the MCT-KD dietary intervention. During the intervention, total fat intake increased (fat: 90.6 g vs. 166.7 g, $p < 0.001$) and total carbohydrate intake was significantly reduced (209.8 g vs. 46.0 g, $p < 0.001$). The mean macronutrient proportion during the dietary intervention was 73.4% fat, 9% carbohydrate and 17.6% protein as energy.

Table 8 Anthropometric, blood-derived and dietary data (n=10)

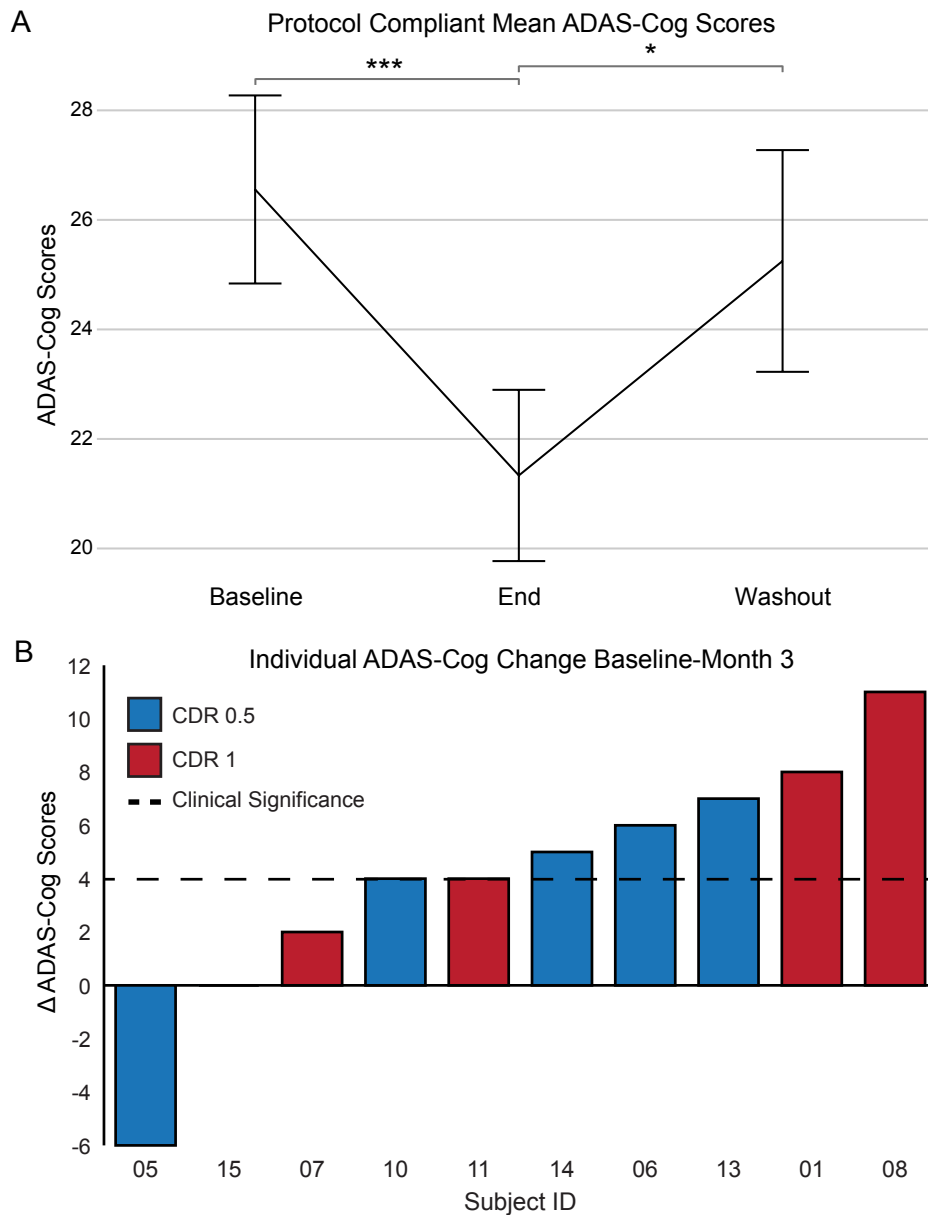
	Pre-KD	Post-KD	P-Value
Anthropometric Measures			
Weight, kg	76.5 (17.4)	74.7 (16.2)	0.81
BMI, kg/m ²	27.7 (7.5)	26.9 (6.8)	0.81
Body Fat, %	38.6 (11.5)	38.2 (11.3)	0.94
Lean Body Mass, kg	43.5 (7.6)	42.8 (8.6)	0.85
Bone Mass, kg	2.7 (0.7)	2.7 (0.7)	0.98
Lipid Status			
Total Cholesterol, mg/dL	173.0 (27.5)	194.4 (36.3)	0.16
LDL, mg/dL	102.1 (18.7)	117.4 (25.4)	0.14
HDL, mg/dL	55.4 (9.2)	58.2 (8.6)	0.49
Serum Biomarkers			
AST, U/L	21.1 (5.2)	24.5 (7.0)	0.24
ALT, U/L	15.7 (6.5)	18.9 (8.1)	0.34
Alkaline Phosphatase, U/L	62.6 (21.3)	55.8 (19.5)	0.48
Calcium, mg/dL	9.4 (0.4)	9.5 (0.3)	0.71
Chloride, mEq/L	104.1 (1.3)	105.4 (2.2)	0.12
Potassium, mEq/L	4.0 (0.3)	4.1 (0.2)	0.47
Sodium, mEq/L	137.2 (1.8)	137.9 (1.9)	0.41
BUN, mg/dL	20.9 (4.3)	20.1 (6.1)	0.74
Creatinine, mg/dL	1.0 (0.2)	1.1 (0.3)	0.58
Metabolic Status			
Insulin, µU/mL	5.1 (2.2)	5.0 (2.2)	0.94
Glucose, mg/dL	92.6 (5.6)	95.8 (10.0)	0.40
HOMA2-IR	0.7 (0.3)	0.7 (0.3)	0.97
Beta, %	67.8 (22.1)	62.3 (19.0)	0.56
Sensitivity, %	169.6 (51.0)	182.3 (86.4)	0.70
Dietary Intake			
Energy (kcal)	1950.7 (450.6)	2002.8 (660.7)	0.80
Fat, g	90.6 (23.5)	166.7 (60.0)	<0.001
Carbohydrate, g	209.8 (80.3)	46.0 (26.9)	<0.001
Protein, g	81.3 (21.1)	90.0 (28.2)	0.34

Cognition

Repeated measures ANOVA was performed to analyze differences in cognitive performance at baseline, month 3 and after the 1-month washout period (Figure 7).

Including all diet compliant participants (n=10), ADAS-Cog scores significantly improved from baseline to month 3 with a mean improvement of 4.1 points (25.5 vs. 21.4, $p=0.02$). Excluding the one protocol non-compliant participant (n=9), ADAS-Cog scores improved from baseline to month 3 with a mean improvement of 5.3 points (26.6 vs. 21.3, $p=0.001$). Improvements in ADAS-Cog scores diminished during the 1-month washout period, with the mean score returning to that similar at baseline (diet compliant [n=10]: 21.4 vs. 25.3, $p=0.09$; excluding protocol non-compliant [n=9]: 21.3 vs. 25.8, $p=0.05$). Excluding the protocol non-compliant participant, MMSE scores significantly improved from baseline to month 3 (25.2 vs. 26.3, $p=0.05$).

Figure 7 Changes in ADAS-Cog scores



A) Mean changes in protocol compliant (n=9) ADAS-Cog scores. Lower ADAS-Cog scores indicate cognition improvement. Scores improved 5.3 points from baseline to month 3. Improvements at month 3 diminished after the 1-month washout period. B) The waterfall plot depicts individual changes in ADAS-Cog scores from baseline to month 3 (end of intervention). One participant declined in cognitive performance. This participant was protocol non-compliant for discontinuing AD medications.

*** $p \leq 0.001$, * $p \leq 0.05$

DISCUSSION

In this pilot trial, we primarily investigated the feasibility and safety of a 3-month medium chain triglyceride ketogenic diet intervention in patients with AD. Secondly, we focused on the effects of the diet on cognition in these patients. The current study found the MCT-KD to be feasible as 10 of the 15 participants achieved elevated urinary and serum ketone levels and adapted to a carbohydrate restrictive and augmented fat nutrient pattern. Furthermore, study finishers achieved the target macronutrient ratio. There were no serious adverse events and laboratory and EKG tests raised no safety concerns. Mean cognition scores for the participants that successfully implemented the MCT-KD improved from baseline to month 3, however, improvements diminished after the 1-month washout period.

Recruitment and compliance for KD studies in adults can be difficult (157-159). Perceptions of the KD border on undesirable, making it difficult to recruit participants via traditional contact methods (i.e. letter, phone call, clinic visit). Based upon the current study's recruitment results, we believe that KD therapy studies in adult populations require unique, interactive recruitment strategies to generate participation interest. Marketing of KD cooking demonstrations generated a great deal more interest and immediately showed recruitment benefit – KD preconceptions were altered by allowing potential participants and study partners to experience a ketogenic meal and enrollment was expedited. It should be noted that limited ketogenic cooking demonstration attendance was due to space limitations rather than generated interest. We are confident that execution of these recruiting strategies will ease recruitment burden for similar future studies.

Five participants withdrew early from the study. These participants were unable to successfully implement the KD, indicating to the study dietitian that no ketones were achieved via urinary ketone testing. One of the early withdrawals was a CDR 0.5 (very mild AD) participant and all 4 CDR 2 (moderate AD) participants withdrew early. Caregivers of the CDR 2 participants conveyed that the stress involved in providing care to patients with such substantial cognitive change is already stressful and that implementing and managing a KD is overwhelming. It is our impression that the MCT-KD may not be feasible in CDR 2 patients, but quite feasible in AD patients with less substantial cognitive change.

Previously reported side effects of the KD include constipation, nausea, vomiting, diarrhea, fatigue and hunger (107). Very few of these symptoms were reported during the diet intervention. The most common complaints were nausea and diarrhea, seemingly induced by the large consumption of MCT oil. A few participants had difficulties titrating to the target MCT dosage, which was resolved by using a blender to emulsify the MCT with a longer chain fatty acid food (most commonly grass-fed butter). Other nausea complaints were resolved through increased consumption of water. No participants complained of hunger or fatigue.

Our pilot data provide compelling evidence that the KD provides beneficial effects on cognition in patients with AD; however, small sample size and single arm design of the current study prevent explicit estimation of the efficacy of the KD treatment on cognition. Only one participant experienced cognitive decline while following the diet protocol, which was the participant considered protocol non-compliant for discontinuing AD medications during the study intervention. Seven participants achieved ADAS-cog

improvements with mean improvement exceeding clinical significance (160). Benefit diminished after a 1-month washout period, suggesting improvement by those on the MCT-KD is unlikely represented by test-retest phenomena; begging the question of how quickly potential cognitive improvement relapses upon discontinuance of the diet. Our data adds to a very small body of evidence that ketogenic therapies may elicit cognitive benefit in individuals with cognition impairment (105, 123).

We've considered several mechanisms that may have driven the cognitive improvements observed in the current study. Brain glucose metabolism deteriorates substantially in patients with AD (26, 34, 35). Recent data suggest that brain ketone metabolism is positively correlated with serum ketone status (121) and may be preserved in the AD brain (35), thus the MCT-KD implemented in the current study may have provided the substrate necessary to compensate for cerebral metabolic deficit. There are indications that the KD affects mitochondrial function on multiple levels (118). The KD has been shown to increase hippocampal mitochondria biogenesis (161). Mitochondrial cytochrome oxidase (COX) activity in neurons is downregulated in AD (26). Unpublished preliminary data from our group demonstrated that neuronal cells increase COX activity when exposed to BHB, which could indicate that ketones induced by the MCT-KD may overcome COX activity reduction. Excessive mitochondrial production of reactive oxygen species (ROS) has also been observed in AD and the KD has been shown to reduce ROS production (124). Furthermore, AD patients exhibit elevation in inflammatory markers and our group observed a marked decrease in brain $\text{TNF}\alpha$ expression in mice fed a KD for 1 month (162).

Cognition improvements through insulin mediated pathways have also been proposed. Previous data, including data from our group, have demonstrated that hyperinsulinemia, insulin resistance and fasting hyperglycemia are associated with brain hypometabolism and AD biomarkers (67, 76, 77). A 6-week trial of carbohydrate restriction in patients with MCI (123) and a 12-week trial of calorie restriction in elderly adults (163) both demonstrated memory improvements that correlated well with reduction in fasting insulin levels. While changes in fasting insulin may elicit cognitive benefit, it is impossible to establish relationships between changes in insulin and cognition from the current study as there was no change in insulin measures and participants did not exhibit hyperinsulinemia at baseline.

KDs appear to have a learning curve as many participants found the diet challenging to implement but the difficulty decreased with practice. Essential resources are necessary for success at the KD, which will be vital for future studies and clinical application of the diet should it be found to be effective in a larger trial. First, a proactive, largely available registered dietitian is necessary for proper implementation and maintenance of the KD. We believe this to be one of the most important cogs in the wheel of this potential therapy's success. The dietitian for the current study remained largely available and maintained frequent contact with participants for support purposes and resolution of diet related issues. Finally, we believe an immediate feedback mechanism, such as urinary ketone testing, is crucial for participants to evaluate ketone status and adjust dietary intake as needed.

A major strength of this study is its novelty of inclusion of AD participants. Another strength involves the elapsed time and washout methodology of cognitive

testing to reduce the risk of test-retest phenomena. The current study also has several limitations. Conclusions from pilot trials are inherently limited by their small sample size. Caution must be exercised in interpretation of cognitive results until a larger efficacy trial is conducted. Furthermore, our interpretation that the KD is not feasible in CDR 2 patients may be pre-emptive due to sample biases.

Our pilot data demonstrated that the MCT-KD is feasible in AD patients in a less advanced stage of the disease and complements previous findings that systemic ketosis may be associated with cognitive improvement in cognitively impaired individuals. Randomized clinical trials powered to assess efficacy of the KD in AD are essential to further investigate KD potential. As treatments for AD are urgently needed, novel therapeutic approaches such as the KD may aid in filling this void.

Chapter Five: Discussion and Conclusions

Summary of Findings

Several important dietary-related findings were discovered in this dissertation. In a sample of 128 cognitively normal individuals, higher intake of high glycemic index foods, sugar and carbohydrate was associated with increased cerebral amyloid burden. Using principal components analysis to establish dietary patterns, a dietary pattern characterized by high glycemic load and sugar intake was strongly associated with cerebral amyloid burden. This is concerning because it is projected that by the year 2050, more than 106 million persons worldwide will have AD (164) and the Western diet (high in carbohydrate, sugar and glycemic load) has become much more prevalent on a global scale (165). Furthermore, higher sugar intake was associated with poorer cognitive performance in this cohort. Next, in a single-arm clinical trial of 15 AD patients that consumed a ketogenic diet for 3 months, the carbohydrate restricted, fat augmented, ketogenic diet was found to be feasible and elicited substantial cognitive improvement. Collectively, manipulating dietary carbohydrate intake may be linked to altering AD risk as well as contribute as a therapeutic intervention for the treatment of AD.

Limitations

The research presented from both studies is novel. Dietary carbohydrate, glycemic load and sugar intake previously had not been directly linked to amyloid burden nor had the ketogenic diet been studied in patients with AD. However, there are some major limitations. First, for the observational study, cross-sectional studies are not designed to establish causal relationships. Second, although accumulation of amyloid is

an identified risk factor for AD, the clinical relevance of amyloid is not precisely understood. Third, for the clinical trial, the trial's power was set up to generate pilot efficacy data, therefore one should take caution in drawing specific conclusions from the study. Finally, there was not control arm included in the study design.

Future Directions

Growing evidence continues to support the hypothesis that Alzheimer's disease is commonly a disease of impaired metabolism. It is vital to understand that behavioral traits such as diet, exercise and sleep habits may be crucial pieces to the puzzle of AD prevention has led to growing interest in this field of study.

As the findings from the observational study presented in this dissertation are the first to directly tie carbohydrate, glycemic load and sugar intake to amyloid burden, further observational studies should be carried out to further investigate the relationship between these dietary components, dietary patterns and amyloid. Beyond this point, it is pertinent to better define amyloid's role in the etiology of AD in order to describe the true meaningfulness of the accumulation of this biomarker and the increase in risk due to the components that affect its processing. Establishment of new and more thorough biomarkers of AD would also be helpful in the advancement of AD prevention studies. Although more difficult, clinical trials that manipulate carbohydrate intake and make-up could potentially be designed to evaluate changes in AD biomarkers and prevention efficacy. There is already a great deal of interest in the Mediterranean diet and DASH diet, which are typically lower in glycemic load than global standard diets (166).

Specifically, clinical trials powered to address efficacy of the ketogenic diet in AD are needed. To date, two pilot trials have shown cognitive benefit in cognitively impaired individuals: 1) a study performed in 12 patients with mild cognitive impairment (123) and 2) the clinical trial presented in this dissertation. Preferably, a trial design would include a more expansive cognitive battery for a more accurate measure of global cognitive changes and potentially tease out changes in cognitive compartments. Additionally, these studies could include PET imaging techniques to measure cerebral glucose and ketone metabolism and elucidate mechanisms by which the ketogenic diet may elicit potential beneficial effects.

Closing Statement

Because changes in glucose metabolism are observed in AD and even prior to diagnosis, the purpose of this research was to better understand how AD is affected by carbohydrate type and manipulation of macronutrient intake. The work from this dissertation suggests that diet is a crucial component in risk of developing AD and may also be utilized as a treatment for those that already have AD. Although much more work is necessary to draw scientific conclusions, this research provides compelling evidence that diet is very likely a modifiable cog in the wheel of the progression of AD.

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Appendix I: Diet History Questionnaire II

This is a sample form. Do not use for scanning.

NATIONAL INSTITUTES OF HEALTH

Diet History Questionnaire II



GENERAL INSTRUCTIONS

- Answer each question as best you can. Estimate if you are not sure. A guess is better than leaving a blank.
- Use only a black ball-point pen. Do not use a pencil or felt-tip pen. Do not fold, staple, or tear the pages.
- Put an X in the box next to your answer.
- If you make any changes, cross out the incorrect answer and put an X in the box next to the correct answer. Also draw a circle around the correct answer.
- If you mark NEVER, NO, or DON'T KNOW for a question, please follow any arrows or instructions that direct you to the next question.

BEFORE TURNING THE PAGE, PLEASE COMPLETE THE FOLLOWING QUESTIONS.

Today's date:

MONTH	DAY	YEAR
<input type="checkbox"/> Jan	<input type="checkbox"/> 0	<input type="checkbox"/> 2010
<input type="checkbox"/> Feb	<input type="checkbox"/> 1	<input type="checkbox"/> 2011
<input type="checkbox"/> Mar	<input type="checkbox"/> 2	<input type="checkbox"/> 2012
<input type="checkbox"/> Apr	<input type="checkbox"/> 3	<input type="checkbox"/> 2013
<input type="checkbox"/> May	<input type="checkbox"/> 4	<input type="checkbox"/> 2014
<input type="checkbox"/> Jun	<input type="checkbox"/> 5	<input type="checkbox"/> 2015
<input type="checkbox"/> Jul	<input type="checkbox"/> 6	<input type="checkbox"/> 2016
<input type="checkbox"/> Aug	<input type="checkbox"/> 7	<input type="checkbox"/> 2017
<input type="checkbox"/> Sep	<input type="checkbox"/> 8	<input type="checkbox"/> 2018
<input type="checkbox"/> Oct	<input type="checkbox"/> 9	<input type="checkbox"/> 2019
<input type="checkbox"/> Nov		<input type="checkbox"/> 2020
<input type="checkbox"/> Dec		

In what month were you born?

<input type="checkbox"/> Jan
<input type="checkbox"/> Feb
<input type="checkbox"/> Mar
<input type="checkbox"/> Apr
<input type="checkbox"/> May
<input type="checkbox"/> Jun
<input type="checkbox"/> Jul
<input type="checkbox"/> Aug
<input type="checkbox"/> Sep
<input type="checkbox"/> Oct
<input type="checkbox"/> Nov
<input type="checkbox"/> Dec

In what year were you born?

19	<input type="checkbox"/> 0	<input type="checkbox"/> 0
	<input type="checkbox"/> 1	<input type="checkbox"/> 1
	<input type="checkbox"/> 2	<input type="checkbox"/> 2
	<input type="checkbox"/> 3	<input type="checkbox"/> 3
	<input type="checkbox"/> 4	<input type="checkbox"/> 4
	<input type="checkbox"/> 5	<input type="checkbox"/> 5
	<input type="checkbox"/> 6	<input type="checkbox"/> 6
	<input type="checkbox"/> 7	<input type="checkbox"/> 7
	<input type="checkbox"/> 8	<input type="checkbox"/> 8
	<input type="checkbox"/> 9	<input type="checkbox"/> 9

Are you male or female?

☐ Male
☐ Female

BAR CODE LABEL OR SUBJECT ID
HERE

DHQ II PastYear

This is a sample form. Do not use for scanning.

1. Over the past 12 months, how often did you drink **carrot juice**?

☐ NEVER (GO TO QUESTION 2)

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2–3 times per day |
| <input type="checkbox"/> 1–2 times per week | <input type="checkbox"/> 4–5 times per day |
| <input type="checkbox"/> 3–4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week | |

1a. Each time you drank **carrot juice**, how much did you usually drink?

- ☐ Less than ½ cup (4 ounces)
☐ ½ to 1¼ cups (4 to 10 ounces)
☐ More than 1¼ cups (10 ounces)

2. Over the past 12 months, how often did you drink **tomato juice** or **other vegetable juice**?
(Please do not include carrot juice.)

☐ NEVER (GO TO QUESTION 3)

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2–3 times per day |
| <input type="checkbox"/> 1–2 times per week | <input type="checkbox"/> 4–5 times per day |
| <input type="checkbox"/> 3–4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week | |

2a. Each time you drank **tomato juice** or **other vegetable juice**, how much did you usually drink?

- ☐ Less than ¾ cup (6 ounces)
☐ ¾ to 1¼ cups (6 to 10 ounces)
☐ More than 1¼ cups (10 ounces)

3. Over the past 12 months, how often did you drink **orange juice** or **grapefruit juice**?

☐ NEVER (GO TO QUESTION 4)

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2–3 times per day |
| <input type="checkbox"/> 1–2 times per week | <input type="checkbox"/> 4–5 times per day |
| <input type="checkbox"/> 3–4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week | |

3a. Each time you drank **orange juice** or **grapefruit juice**, how much did you usually drink?

- ☐ Less than ¾ cup (6 ounces)
☐ ¾ to 1¼ cups (6 to 10 ounces)
☐ More than 1¼ cups (10 ounces)

Question 4 appears in the next column

3b. How often was the orange juice or grapefruit juice you drank **calcium-fortified**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

4. Over the past 12 months, how often did you drink **other 100% fruit juice** or **100% fruit juice mixtures** (such as apple, grape, pineapple, or others)?

☐ NEVER (GO TO QUESTION 5)

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2–3 times per day |
| <input type="checkbox"/> 1–2 times per week | <input type="checkbox"/> 4–5 times per day |
| <input type="checkbox"/> 3–4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week | |

4a. Each time you drank **other 100% fruit juice** or **100% fruit juice mixtures**, how much did you usually drink?

- ☐ Less than ¾ cup (6 ounces)
☐ ¾ to 1¼ cups (6 to 12 ounces)
☐ More than 1¼ cups (12 ounces)

4b. How often were the other 100% fruit juice or 100% fruit juice mixtures you drank **calcium-fortified**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

5. How often did you drink **other fruit drinks** (such as cranberry cocktail, Hi-C, lemonade, or Kool-Aid, diet or regular)?

☐ NEVER (GO TO QUESTION 6)

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2–3 times per day |
| <input type="checkbox"/> 1–2 times per week | <input type="checkbox"/> 4–5 times per day |
| <input type="checkbox"/> 3–4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week | |

Question 6 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

- 5a. Each time you drank **fruit drinks**, how much did you usually drink?
- ☐ Less than 1 cup (8 ounces)
☐ 1 to 2 cups (8 to 16 ounces)
☐ More than 2 cups (16 ounces)
- 5b. How often were your fruit drinks **diet** or **sugar-free**?
- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always
6. How often did you drink **milk as a beverage** (NOT in coffee, NOT in cereal)? *(Please do not include chocolate milk and hot chocolate.)*
- ☐ NEVER (GO TO QUESTION 7)
- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2–3 times per day |
| <input type="checkbox"/> 1–2 times per week | <input type="checkbox"/> 4–5 times per day |
| <input type="checkbox"/> 3–4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week | |
- 6a. Each time you drank **milk as a beverage**, how much did you usually drink?
- ☐ Less than 1 cup (8 ounces)
☐ 1 to 1½ cups (8 to 12 ounces)
☐ More than 1½ cups (12 ounces)
- 6b. What kind of **milk** did you usually drink?
- ☐ Whole milk
☐ 2% fat milk
☐ 1 % fat milk
☐ Skim, nonfat, or ½% fat milk
☐ Soy milk
☐ Rice milk
☐ Other
7. How often did you drink **chocolate milk** (including hot chocolate)?
- ☐ NEVER (GO TO QUESTION 8)
- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2–3 times per day |
| <input type="checkbox"/> 1–2 times per week | <input type="checkbox"/> 4–5 times per day |
| <input type="checkbox"/> 3–4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week | |

Question 8 appears in the next column

- 7a. Each time you drank **chocolate milk**, how much did you usually drink?
- ☐ Less than 1 cup (8 ounces)
☐ 1 to 1½ cups (8 to 12 ounces)
☐ More than 1½ cups (12 ounces)
- 7b. How often was the chocolate milk **reduced-fat** or **fat-free**?
- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

8. How often did you drink **meal replacement** or **high-protein beverages** (such as Instant Breakfast, Ensure, Slimfast, Sustacal or others)?
- ☐ NEVER (GO TO QUESTION 9)
- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2–3 times per day |
| <input type="checkbox"/> 1–2 times per week | <input type="checkbox"/> 4–5 times per day |
| <input type="checkbox"/> 3–4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week | |

- 8a. Each time you drank **meal replacement** or **high-protein beverages**, how much did you usually drink?
- ☐ Less than 1 cup (8 ounces)
☐ 1 to 1½ cups (8 to 12 ounces)
☐ More than 1½ cups (12 ounces)

9. Over the past 12 months, did you drink **soda** or **pop**?

☐ NO (GO TO QUESTION 10)

☐ YES

- 9a. How often did you drink **soda** or **pop** **IN THE SUMMER**?
- ☐ NEVER
- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2–3 times per day |
| <input type="checkbox"/> 1–2 times per week | <input type="checkbox"/> 4–5 times per day |
| <input type="checkbox"/> 3–4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5–6 times per week | |

Question 10 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

9b. How often did you drink **soda** or **pop**
DURING THE REST OF THE YEAR?

☐ NEVER

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

9c. Each time you drank **soda** or **pop**, how much did you usually drink?

- ☐ Less than 12 ounces or less than 1 can or bottle
☐ 12 to 16 ounces or 1 can or bottle
☐ More than 16 ounces or more than 1 can or bottle

9d. How often were these sodas or pop **diet** or **sugar-free**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

9e. How often were these sodas or pop **caffeine-free**?

- ☐ Almost never or never
☐ About 1/4 of the time
☐ About 1/2 of the time
☐ About 3/4 of the time
☐ Almost always or always

10. Over the past 12 months, did you drink **sports drinks** (such as Propel, PowerAde, or Gatorade)?

☐ NO (GO TO QUESTION 11)

☒ YES

10a. How often did you drink **sports drinks** **IN THE SUMMER?**

☐ NEVER

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

Question 11 appears in the next column

10b. How often did you drink **sports drinks**
DURING THE REST OF THE YEAR?

☐ NEVER

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

10c. Each time you drank **sports drinks**, how much did you usually drink?

- ☐ Less than 12 ounces or less than 1 bottle
☐ 12 to 24 ounces or 1 to 2 bottles
☐ More than 24 ounces or more than 2 bottles

11. Over the past 12 months, did you drink **energy drinks** (such as Red Bull or Jolt)?

☐ NO (GO TO QUESTION 12)

☒ YES

11a. How often did you drink **energy drinks** **IN THE SUMMER?**

☐ NEVER

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

11b. How often did you drink **energy drinks**
DURING THE REST OF THE YEAR?

☐ NEVER

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

11c. Each time you drank **energy drinks**, how much did you usually drink?

- ☐ Less than 8 ounces or less than 1 cup
☐ 8 to 16 ounces or 1 to 2 cups
☐ More than 16 ounces or more than 2 cups

Question 12 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

12. Over the past 12 months, did you drink **beer**?

☐ NO (GO TO QUESTION 13)

☒ YES

12a. How often did you drink **beer** **IN THE SUMMER**?

☐ NEVER

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

12b. How often did you drink **beer** **DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

12c. Each time you drank **beer**, how much did you usually drink?

- ☐ Less than a 12-ounce can or bottle
☐ 1 to 3 12-ounce cans or bottles
☐ More than 3 12-ounce cans or bottles



13. Over the past 12 months, did you drink **water** (including tap, bottled, and carbonated water)?

☐ NO (GO TO QUESTION 14)

☒ YES

13a. How often did you drink **water** (including tap, bottled, and carbonated water) **IN THE SUMMER**?

☐ NEVER

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

Question 14 appears in the next column

13b. How often did you drink **water** (including tap, bottled, and carbonated water) **DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

13c. Each time you drank **water**, how much did you usually drink?

- ☐ Less than 12 ounces or less than 1 bottle
☐ 12 to 24 ounces or 1 to 2 bottles
☐ More than 24 ounces or more than 2 bottles

13d. How often was the water you drank **tap water**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

13e. How often was the water you drank **bottled, sweetened water** (with low or no-calorie sweetener, including carbonated water)?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

13f. How often was the water you drank **bottled, unsweetened water** (including carbonated water)?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

14. How often did you drink **wine** or **wine coolers**?

☐ NEVER (GO TO QUESTION 15)

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

Question 15 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

14a. Each time you drank **wine** or **wine coolers**, how much did you usually drink?

- ☐ Less than 5 ounces or less than 1 glass
☐ 5 to 12 ounces or 1 to 2 glasses
☐ More than 12 ounces or more than 2 glasses

15. How often did you drink **liquor** or **mixed drinks**?

☐ NEVER (GO TO QUESTION 16)

- | | |
|---|--|
| <input type="checkbox"/> 1 time per month or less | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 2-3 times per day |
| <input type="checkbox"/> 1-2 times per week | <input type="checkbox"/> 4-5 times per day |
| <input type="checkbox"/> 3-4 times per week | <input type="checkbox"/> 6 or more times per day |
| <input type="checkbox"/> 5-6 times per week | |

15a. Each time you drank **liquor** or **mixed drinks**, how much did you usually drink?

- ☐ Less than 1 shot of liquor
☐ 1 to 3 shots of liquor
☐ More than 3 shots of liquor

16. Over the past 12 months, did you eat **oatmeal**, **grits**, or **other cooked cereal**?

☐ NO (GO TO QUESTION 17)

☐ YES

16a. How often did you eat **oatmeal**, **grits**, or **other cooked cereal IN THE WINTER**?

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per winter | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per winter | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

16b. How often did you eat **oatmeal**, **grits**, or **other cooked cereal DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 17 appears in the next column

16c. Each time you ate **oatmeal**, **grits**, or **other cooked cereal**, how much did you usually eat?

- ☐ Less than ¼ cup
☐ ¼ to 1¼ cups
☐ More than 1¼ cups

16d. How often was **butter** or **margarine** added to your oatmeal, grits or other cooked cereal?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

17. How often did you eat **cold cereal**?

☐ NEVER (GO TO QUESTION 18)

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

17a. Each time you ate **cold cereal**, how much did you usually eat?

- ☐ Less than 1 cup
☐ 1 to 2½ cups
☐ More than 2½ cups

17b. How often was the cold cereal you ate **Total Raisin Bran**, **Total Cereal**, or **Product 19**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

17c. How often was the cold cereal you ate **All Bran**, **Fiber One**, **100% Bran**, or **All-Bran Bran Buds**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 18 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months**...

17d. How often was the cold cereal you ate **some other bran or fiber cereal** (such as Cheerios, Shredded Wheat, Raisin Bran, Bran Flakes, Grape-Nuts, Granola, Wheaties, or Healthy Choice)?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

17e. How often was the cold cereal you ate any **other type of cold cereal** (such as Corn Flakes, Rice Krispies, Frosted Flakes, Special K, Froot Loops, Cap'n Crunch, or others)?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

17f. Was **milk** added to your cold cereal?

☐ NO (GO TO QUESTION 18)

☐ YES

17g. What kind of **milk** was usually added?

- ☐ Whole milk
☐ 2% fat milk
☐ 1% fat milk
☐ Skim, nonfat, or ½% fat milk
☐ Soy milk
☐ Rice milk
☐ Other

17h. Each time **milk was added to your cold cereal**, how much was usually added?

- ☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

18. How often did you eat **applesauce**?

☐ NEVER (GO TO QUESTION 19)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 19 appears in the next column

18a. Each time you ate **applesauce**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

19. How often did you eat **apples**?

☐ NEVER (GO TO QUESTION 20)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

19a. Each time you ate **apples**, how many did you usually eat?

- ☐ Less than 1 apple
☐ 1 apple
☐ More than 1 apple

20. How often did you eat **pears** (fresh, canned, or frozen)?

☐ NEVER (GO TO QUESTION 21)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

20a. Each time you ate **pears**, how many did you usually eat?

- ☐ Less than 1 pear
☐ 1 pear
☐ More than 1 pear

21. How often did you eat **bananas**?

☐ NEVER (GO TO QUESTION 22)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |



Question 22 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

21a. Each time you ate **bananas**, how many did you usually eat?

- ☐ Less than 1 banana
☐ 1 banana
☐ More than 1 banana

22. How often did you eat **dried fruit** (such as prunes or raisins)? *(Please do not include dried apricots.)*

☐ NEVER (GO TO QUESTION 23)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

22a. Each time you ate **dried fruit**, how much did you usually eat?

- ☐ Less than 2 tablespoons
☐ 2 to 5 tablespoons
☐ More than 5 tablespoons

23. Over the past 12 months, did you eat **peaches, nectarines, or plums**?

☐ NO (GO TO QUESTION 24)

☐ YES

23a. How often did you eat **fresh peaches, nectarines, or plums WHEN IN SEASON**?

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per season | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

23b. How often did you eat **peaches, nectarines, or plums** (fresh, canned, or frozen) **DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 24 appears in the next column

23c. Each time you ate **peaches, nectarines, or plums**, how much did you usually eat?

- ☐ Less than 1 fruit or less than ½ cup
☐ 1 to 2 fruits or ½ to ¾ cup
☐ More than 2 fruits or more than ¾ cup

24. How often did you eat **grapes**?

☐ NEVER (GO TO QUESTION 25)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

24a. Each time you ate **grapes**, how much did you usually eat?

- ☐ Less than ½ cup or less than 10 grapes
☐ ½ to 1 cup or 10 to 30 grapes
☐ More than 1 cup or more than 30 grapes

25. Over the past 12 months, did you eat **cantaloupe**?

☐ NO (GO TO QUESTION 26)

☐ YES

25a. How often did you eat **fresh cantaloupe WHEN IN SEASON**?

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per season | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

25b. How often did you eat **cantaloupe** (fresh or frozen) **DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 26 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

25c. Each time you ate **cantaloupe**, how much did you usually eat?

- ☐ Less than ¼ melon or less than ½ cup
☐ ¼ melon or ½ to 1 cup
☐ More than ¼ melon or more than 1 cup

26. Over the past 12 months, did you eat **melon, other than cantaloupe** (such as watermelon or honeydew)?

☐ NO (GO TO QUESTION 27)

↓ ☐ YES

26a. How often did you eat **fresh melon, other than cantaloupe, WHEN IN SEASON?**

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per season | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

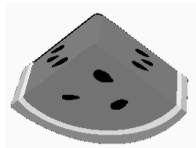
26b. How often did you eat **melon other than cantaloupe** (fresh or frozen) **DURING THE REST OF THE YEAR?**

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

26c. Each time you ate **melon other than cantaloupe**, how much did you usually eat?

- ☐ Less than ½ cup or 1 small wedge
☐ ½ to 2 cups or 1 medium wedge
☐ More than 2 cups or 1 large wedge



Question 27 appears in the next column

27. Over the past 12 months, did you eat **strawberries**?

☐ NO (GO TO QUESTION 28)

↓ ☐ YES

27a. How often did you eat **fresh strawberries WHEN IN SEASON?**

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per season | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

27b. How often did you eat **strawberries** (fresh or frozen) **DURING THE REST OF THE YEAR?**

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

27c. Each time you ate **strawberries**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 3 berries
☐ ¼ to ¾ cup or 3 to 8 berries
☐ More than ¾ cup or more than 8 berries

28. Over the past 12 months, did you eat **oranges, tangerines, or clementines**?

☐ NO (GO TO QUESTION 29)

↓ ☐ YES

28a. How often did you eat **fresh oranges, tangerines, or clementines WHEN IN SEASON?**

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per season | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 29 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

28b. How often did you eat **oranges, tangerines, or clementines** (fresh or canned) **DURING THE REST OF THE YEAR?**

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

28c. Each time you ate **oranges, tangerines, or clementines**, how many did you usually eat?

- ☐ Less than 1 fruit
☐ 1 fruit
☐ More than 1 fruit

29. Over the past 12 months, did you eat **grapefruit**?

☐ NO (GO TO QUESTION 30)

☐ YES

29a. How often did you eat **fresh grapefruit WHEN IN SEASON?**

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per season | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

29b. How often did you eat **grapefruit** (fresh or canned) **DURING THE REST OF THE YEAR?**

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 30 appears in the next column

29c. Each time you ate **grapefruit**, how much did you usually eat?

- ☐ Less than ½ grapefruit
☐ ½ grapefruit
☐ More than ½ grapefruit

30. How often did you eat **pineapple**?

☐ NEVER (GO TO QUESTION 31)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

30a. Each time you ate **pineapple**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 1 medium slice
☐ ¼ to ¾ cup or 1 medium slice
☐ More than ¾ cup or more than 1 medium slice

31. How often did you eat **other kinds of fruit**?

☐ NEVER (GO TO QUESTION 32)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

31a. Each time you ate **other kinds of fruit**, how much did you usually eat?

- ☐ Less than ¼ cup
☐ ¼ to ¾ cup
☐ More than ¾ cup

32. How often did you eat **COOKED greens** (such as spinach, turnip, collard, mustard, chard, or kale)?

☐ NEVER (GO TO QUESTION 33)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 33 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months...**

32a. Each time you ate **COOKED greens**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

33. How often did you eat **RAW greens** (such as spinach, turnip, collard, mustard, chard, or kale)? (*We will ask about lettuce later.*)

☐ NEVER (GO TO QUESTION 34)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

33a. Each time you ate **RAW greens**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

34. How often did you eat **coleslaw**?

☐ NEVER (GO TO QUESTION 35)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

34a. Each time you ate **coleslaw**, how much did you usually eat?

- ☐ Less than ¼ cup
☐ ¼ to ¾ cup
☐ More than ¾ cup

35. How often did you eat **sauerkraut** or **cabbage** (other than coleslaw)?

☐ NEVER (GO TO QUESTION 36)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 36 appears in the next column

35a. Each time you ate **sauerkraut** or **cabbage**, how much did you usually eat?

- ☐ Less than ¼ cup
☐ ¼ to 1 cup
☐ More than 1 cup

36. How often did you eat **carrots** (fresh, canned, or frozen)?

☐ NEVER (GO TO QUESTION 37)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

36a. Each time you ate **carrots**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 2 baby carrots
☐ ¼ to ½ cup or 2 to 5 baby carrots
☐ More than ½ cup or more than 5 baby carrots

37. How often did you eat **string beans** or **green beans** (fresh, canned, or frozen)?

☐ NEVER (GO TO QUESTION 38)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

37a. Each time you ate **string beans** or **green beans**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

38. How often did you eat **peas** (fresh, canned, or frozen)?

☐ NEVER (GO TO QUESTION 39)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 39 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

38a. Each time you ate **peas**, how much did you usually eat?

- ☐ Less than ¼ cup
☐ ¼ to ¾ cup
☐ More than ¾ cup

39. Over the past 12 months, did you eat **corn**?

☐ NO (GO TO QUESTION 40)

☐ YES

39a. How often did you eat **fresh corn WHEN IN SEASON**?

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per season | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per season | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

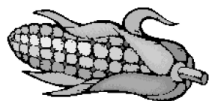
39b. How often did you eat **corn** (fresh, canned, or frozen) **DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

39c. Each time you ate **corn**, how much did you usually eat?

- ☐ Less than 1 ear or less than ½ cup
☐ 1 ear or ½ to 1 cup
☐ More than 1 ear or more than 1 cup



Question 40 appears in the next column

40. How often did you eat **broccoli** (fresh or frozen)?

☐ NEVER (GO TO QUESTION 41)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

40a. Each time you ate **broccoli**, how much did you usually eat?

- ☐ Less than ¼ cup
☐ ¼ to 1 cup
☐ More than 1 cup

41. How often did you eat **cauliflower or Brussels sprouts** (fresh or frozen)?

☐ NEVER (GO TO QUESTION 42)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

41a. Each time you ate **cauliflower or Brussels sprouts**, how much did you usually eat?

- ☐ Less than ¼ cup
☐ ¼ to ½ cup
☐ More than ½ cup

42. How often did you eat **asparagus** (fresh or frozen)?

☐ NEVER (GO TO QUESTION 43)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

42a. Each time you ate **asparagus**, how much did you usually eat?

- ☐ Less than ½ cup or less than 4 spears
☐ ½ to ¾ cup or 4 to 7 spears
☐ More than ¾ cup or more than 7 spears

Question 43 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months...**

43. How often did you eat **winter squash** (such as pumpkin, butternut, or acorn)?

- ☐ NEVER (GO TO QUESTION 44)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

43a. Each time you ate **winter squash**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to ¾ cup
☐ More than ¾ cup

44. How often did you eat **mixed vegetables**?

- ☐ NEVER (GO TO QUESTION 45)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

44a. Each time you ate **mixed vegetables**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

45. How often did you eat **onions**?

- ☐ NEVER (GO TO QUESTION 46)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

45a. Each time you ate **onions**, how much did you usually eat?

- ☐ Less than 1 slice or less than 1 tablespoon
☐ 1 slice or 1 to 4 tablespoons
☐ More than 1 slice or more than 4 tablespoons

Question 46 appears in the next column

46. Now think about all the **cooked vegetables** you ate in the **past 12 months** and how they were prepared. How often were your vegetables **COOKED WITH** some sort of **fat**, including oil spray? (*Please do not include potatoes.*)

- ☐ NEVER (GO TO QUESTION 47)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |



46a. Which fats were usually added to your vegetables **DURING COOKING**? (*Please do not include potatoes. Mark all that apply.*)

- | | |
|--|---|
| <input type="checkbox"/> Margarine (including low-fat) | <input type="checkbox"/> Corn oil |
| <input type="checkbox"/> Butter (including low-fat) | <input type="checkbox"/> Canola or rapeseed oil |
| <input type="checkbox"/> Lard, fatback, or bacon fat | <input type="checkbox"/> Oil spray, such as Pam or others |
| <input type="checkbox"/> Olive oil | <input type="checkbox"/> Other kinds of oils |
| | <input type="checkbox"/> None of the above |

47. Now, thinking again about all the **cooked vegetables** you ate in the **past 12 months**, how often was some sort of fat, sauce, or dressing added **AFTER COOKING OR AT THE TABLE**? (*Please do not include potatoes.*)

- ☐ NEVER (GO TO QUESTION 48)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 2 times per day |
| <input type="checkbox"/> 1–2 times per week | <input type="checkbox"/> 3 or more times per day |

Question 48 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

47a. Which fats, sauces, or dressings were usually added **AFTER COOKING OR AT THE TABLE**? (Please do not include potatoes. **Mark all that apply.**)

- | | |
|--|---|
| <input type="checkbox"/> Margarine (including low-fat) | <input type="checkbox"/> Salad dressing |
| <input type="checkbox"/> Butter (including low-fat) | <input type="checkbox"/> Cheese sauce |
| <input type="checkbox"/> Lard, fatback, or bacon fat | <input type="checkbox"/> White sauce |
| | <input type="checkbox"/> Other |

47b. If margarine, butter, lard, fatback, or bacon fat was added to your cooked vegetables **AFTER COOKING OR AT THE TABLE**, how much did you usually add?

- ☐ Did not usually add these
☐ Less than 1 teaspoon
☐ 1 to 3 teaspoons
☐ More than 3 teaspoons

47c. If salad dressing, cheese sauce, or white sauce was added to your cooked vegetables **AFTER COOKING OR AT THE TABLE**, how much did you usually add?

- ☐ Did not usually add these
☐ Less than 1 tablespoon
☐ 1 to 3 tablespoons
☐ More than 3 tablespoons

48. How often did you eat **sweet peppers** (green, red, or yellow)?

☐ NEVER (GO TO QUESTION 49)

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

48a. Each time you ate **sweet peppers**, how much did you usually eat?

- ☐ Less than 1/8 pepper
☐ 1/8 to 1/4 pepper
☐ More than 1/4 pepper

Question 49 appears in the next column

49. Over the past 12 months, did you eat **fresh tomatoes** (including those in salads)?

☐ NO (GO TO QUESTION 50)

☐ YES

49a. How often did you eat **fresh tomatoes** (including those in salads) **WHEN IN SEASON**?

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per season | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per season | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

49b. How often did you eat **fresh tomatoes** (including those in salads) **DURING THE REST OF THE YEAR**?

☐ NEVER

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

49c. Each time you ate **fresh tomatoes**, how much did you usually eat?

- ☐ Less than 1/4 tomato
☐ 1/4 to 1/2 tomato
☐ More than 1/2 tomato

50. How often did you eat **lettuce salads** (with or without other vegetables)?

☐ NEVER (GO TO QUESTION 51)

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 51 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months**...

50a. Each time you ate **lettuce salads**, how much did you usually eat?

- ☐ Less than ¼ cup
☐ ¼ to 1¼ cups
☐ More than 1¼ cups

50b. How often did the lettuce salads you ate include **dark green lettuce**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

51. How often did you eat **salad dressing** (including low-fat) **on salads**?

☐ NEVER (GO TO QUESTION 52)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

51a. Each time you ate **salad dressing on salads**, how much did you usually eat?

- ☐ Less than 2 tablespoons
☐ 2 to 4 tablespoons
☐ More than 4 tablespoons

52. How often did you eat **sweet potatoes** or **yams**?

☐ NEVER (GO TO QUESTION 53)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

52a. Each time you ate **sweet potatoes** or **yams**, how much did you usually eat?

- ☐ 1 small potato or less than ¼ cup
☐ 1 medium potato or ¼ to ¾ cup
☐ 1 large potato or more than ¾ cup

Question 53 appears in the next column

53. How often did you eat **French fries, home fries, hash browned potatoes, or tater tots**?

☐ NEVER (GO TO QUESTION 54)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

53a. Each time you ate **French fries, home fries, hash browned potatoes, or tater tots** how much did you usually eat?

- ☐ Less than 10 fries or less than ½ cup
☐ 10 to 25 fries or ½ to 1 cup
☐ More than 25 fries or more than 1 cup

54. How often did you eat **potato salad**?

☐ NEVER (GO TO QUESTION 55)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

54a. Each time you ate **potato salad**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

55. How often did you eat **baked, boiled, or mashed potatoes**?

☐ NEVER (GO TO QUESTION 56)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

55a. Each time you ate **baked, boiled, or mashed potatoes**, how much did you usually eat?

- ☐ 1 small potato or less than ¼ cup
☐ 1 medium potato or ¼ to 1 cup
☐ 1 large potato or more than 1 cup

Question 56 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months...**

55b. How often was **sour cream** (including low-fat) added to your potatoes, **EITHER IN COOKING OR AT THE TABLE?**

- ☐ Almost never or never (GO TO QUESTION 55d)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

55c. Each time **sour cream** was added to your potatoes, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 3 tablespoons
- ☐ More than 3 tablespoons

55d. How often was **margarine** (including low-fat) added to your potatoes, **EITHER IN COOKING OR AT THE TABLE?**

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

55e. How often was **butter** (including low-fat) added to your potatoes, **EITHER IN COOKING OR AT THE TABLE?**

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

55f. Each time **margarine** or **butter** was added to your potatoes, how much was usually added?

- ☐ Never added
- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

55g. How often was **cheese** or **cheese sauce** added to your potatoes, **EITHER IN COOKING OR AT THE TABLE?**

- ☐ Almost never or never (GO TO QUESTION 56)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 56 appears in the next column

55h. Each time **cheese** or **cheese sauce** was added to your potatoes, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 3 tablespoons
- ☐ More than 3 tablespoons

56. How often did you eat **salsa**?

- ☐ NEVER (GO TO QUESTION 57)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

56a. Each time you ate **salsa**, how much did you usually eat?

- ☐ Less than 1 tablespoon
- ☐ 1 to 5 tablespoons
- ☐ More than 5 tablespoons

57. How often did you eat **catsup**?

- ☐ NEVER (GO TO QUESTION 58)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

57a. Each time you ate **catsup**, how much did you usually eat?

- ☐ Less than 1 teaspoon
- ☐ 1 to 6 teaspoons
- ☐ More than 6 teaspoons

58. How often did you eat **stuffing, dressing, or dumplings**?

- ☐ NEVER (GO TO QUESTION 59)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

58a. Each time you ate **stuffing, dressing, or dumplings**, how much did you usually eat?

- ☐ Less than ½ cup
- ☐ ½ to 1 cup
- ☐ More than 1 cup

Question 59 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

59. How often did you eat **chili**?

- ☐ NEVER (GO TO QUESTION 60)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

59a. Each time you ate **chili**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1¼ cups
☐ More than 1¼ cups

60. How often did you eat **Mexican foods** (such as tacos, tostados, burritos, tamales, fajitas, enchiladas, quesadillas, and chimichangas)?

- ☐ NEVER (GO TO QUESTION 61)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

60a. Each time you ate **Mexican foods**, how much did you usually eat?

- ☐ Less than 1 taco, burrito, etc.
☐ 1 to 2 tacos, burritos, etc.
☐ More than 2 tacos, burritos, etc.

61. How often did you eat **cooked dried beans** (such as baked beans, pintos, kidney, blackeyed peas, lima, lentils, soybeans, or refried beans)? *(Please do not include bean soups or chili.)*

- ☐ NEVER (GO TO QUESTION 62)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

61a. Each time you ate **beans**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

Question 62 appears in the next column

61b. How often were the beans you ate **refried beans, beans prepared with any type of fat, or with meat added**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

62. How often did you eat **other kinds of vegetables**?

- ☐ NEVER (GO TO QUESTION 63)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

62a. Each time you ate **other kinds of vegetables**, how much did you usually eat?

- ☐ Less than ¼ cup
☐ ¼ to ½ cup
☐ More than ½ cup

63. How often did you eat **rice or other cooked grains** (such as bulgur, cracked wheat, or millet)?

- ☐ NEVER (GO TO QUESTION 64)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

63a. Each time you ate **rice or other cooked grains**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1½ cups
☐ More than 1½ cups

63b. How often was **butter, margarine, or oil** added to your rice or other cooked grains **IN COOKING OR AT THE TABLE**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 64 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months...**

64. How often did you eat **pancakes, waffles, or French toast**?

☐ NEVER (GO TO QUESTION 65)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

64a. Each time you ate **pancakes, waffles, or French toast**, how much did you usually eat?

- ☐ Less than 1 medium piece
☐ 1 to 3 medium pieces
☐ More than 3 medium pieces

64b. How often was **margarine** (including low-fat) added to your pancakes, waffles, or French toast **AFTER COOKING OR AT THE TABLE**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

64c. How often was **butter** (including low-fat) added to your pancakes, waffles, or French toast **AFTER COOKING OR AT THE TABLE**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

64d. Each time **margarine** or **butter** was added to your pancakes, waffles, or French toast, how much was usually added?

- ☐ Never added
☐ Less than 1 teaspoon
☐ 1 to 3 teaspoons
☐ More than 3 teaspoons

64e. How often was **syrup** added to your pancakes, waffles, or French toast?

- ☐ Almost never or never (GO TO QUESTION 65)
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 65 appears in the next column

64f. Each time **syrup** was added to your pancakes, waffles, or French toast, how much was usually added?

- ☐ Less than 1 tablespoon
☐ 1 to 4 tablespoons
☐ More than 4 tablespoons

65. How often did you eat **lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini**?
(Please do not include spaghetti or other pasta.)

☐ NEVER (GO TO QUESTION 66)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

65a. Each time you ate **lasagna, stuffed shells, stuffed manicotti, ravioli, or tortellini**, how much did you usually eat?

- ☐ Less than 1 cup
☐ 1 to 2 cups
☐ More than 2 cups

66. How often did you eat **macaroni and cheese**?

☐ NEVER (GO TO QUESTION 67)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

66a. Each time you ate **macaroni and cheese**, how much did you usually eat?

- ☐ Less than 1 cup
☐ 1 to 1½ cups
☐ More than 1½ cups

67. How often did you eat **pasta salad** or **macaroni salad**?

☐ NEVER (GO TO QUESTION 68)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 68 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months...**

67a. Each time you ate **pasta salad** or **macaroni salad**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

68. Other than the pastas listed in Questions 65, 66, and 67, how often did you eat **pasta, spaghetti, or other noodles**?

☐ NEVER (GO TO QUESTION 69)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

68a. Each time you ate **pasta, spaghetti, or other noodles**, how much did you usually eat?

- ☐ Less than 1 cup
☐ 1 to 3 cups
☐ More than 3 cups

68b. How often did you eat your pasta, spaghetti, or other noodles with **tomato sauce** or **spaghetti sauce made WITH meat**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

68c. How often did you eat your pasta, spaghetti, or other noodles with **tomato sauce** or **spaghetti sauce made WITHOUT meat**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

68d. How often did you eat your pasta, spaghetti, or other noodles with **margarine, butter, oil, or cream sauce**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 69 appears in the next column

69. How often did you eat **bagels** or **English muffins**?

☐ NEVER (GO TO INTRODUCTION TO QUESTION 70)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

69a. How often were the bagels or English muffins you ate **whole wheat**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

69b. Each time you ate **bagels** or **English muffins**, how many did you usually eat?

- ☐ Less than 1 bagel or English muffin
☐ 1 bagel or English muffin
☐ More than 1 bagel or English muffin

69c. How often was **margarine** (including low-fat) added to your bagels or English muffins?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

69d. How often was **butter** (including low-fat) added to your bagels or English muffins?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

69e. Each time **margarine** or **butter** was added to your bagels or English muffins, how much was usually added?

- ☐ Never added
☐ Less than 1 teaspoon
☐ 1 to 2 teaspoons
☐ More than 2 teaspoons

Introduction to Question 70 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months**...

69f. How often was **cream cheese** (including low-fat) spread on your bagels or English muffins?

- ☐ Almost never or never (GO TO INTRODUCTION TO QUESTION 70)
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

69g. Each time **cream cheese** was added to your bagels or English muffins, how much was usually added?

- ☐ Less than 1 tablespoon
☐ 1 to 2 tablespoons
☐ More than 2 tablespoons

The next questions ask about your intake of breads other than bagels or English muffins. First, we will ask about bread you ate as part of sandwiches only. Then we will ask about all other bread you ate.

70. How often did you eat **breads or rolls AS PART OF SANDWICHES** (including burger and hot dog rolls)?
(Please do not include fast food sandwiches.)

- ☐ NEVER (GO TO QUESTION 71)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

70a. Each time you ate **breads or rolls AS PART OF SANDWICHES**, how many did you usually eat?

- ☐ 1 slice or ½ roll
☐ 2 slices or 1 roll
☐ More than 2 slices or more than 1 roll

70b. How often were the breads or rolls that you used for your sandwiches **white bread** (including burger and hot dog rolls)?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 71 appears in the next column

70c. How often was **mayonnaise** or **mayonnaise-type dressing** (including low-fat) added to the breads or rolls used for your sandwiches?

- ☐ Almost never or never (GO TO QUESTION 70e)
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

70d. Each time **mayonnaise** or **mayonnaise-type dressing** was added to the breads or rolls used for your sandwiches, how much was usually added?

- ☐ Less than 1 teaspoon
☐ 1 to 3 teaspoons
☐ More than 3 teaspoons

70e. How often was **margarine** (including low-fat) added to the breads or rolls used for your sandwiches?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

70f. How often was **butter** (including low-fat) added to the breads or rolls used for your sandwiches?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

70g. Each time **margarine** or **butter** was added to the breads or rolls used for your sandwiches, how much was usually added?

- ☐ Never added
☐ Less than 1 teaspoon
☐ 1 to 2 teaspoons
☐ More than 2 teaspoons

71. How often did you eat **breads or dinner rolls, NOT AS PART OF SANDWICHES**?

- ☐ NEVER (GO TO QUESTION 72)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 72 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months...**

71a. Each time you ate **bread**s or **dinner rolls**, **NOT AS PART OF SANDWICHES**, how much did you usually eat?

- ☐ 1 slice or 1 dinner roll
- ☐ 2 slices or 2 dinner rolls
- ☐ More than 2 slices or 2 dinner rolls

71b. How often were the breads or rolls you ate **white bread**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

71c. How often was **margarine** (including low-fat) added to your breads or rolls?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

71d. How often was **butter** (including low-fat) added to your breads or rolls?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

71e. Each time **margarine** or **butter** was added to your breads or rolls, how much was usually added?

- ☐ Never added
- ☐ Less than 1 teaspoon
- ☐ 1 to 2 teaspoons
- ☐ More than 2 teaspoons

71f. How often was **cream cheese** (including low-fat) added to your breads or rolls?

- ☐ Almost never or never (GO TO QUESTION 72)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 72 appears in the next column

71g. Each time **cream cheese** was added to your breads or rolls, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 2 tablespoons
- ☐ More than 2 tablespoons

72. How often did you eat **jam, jelly**, or **honey** on bagels, muffins, bread, rolls, or crackers?

- ☐ NEVER (GO TO QUESTION 73)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

72a. Each time you ate **jam, jelly**, or **honey**, how much did you usually eat?

- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

73. How often did you eat **peanut butter** or **other nut butter**?

- ☐ NEVER (GO TO QUESTION 74)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

73a. Each time you ate **peanut butter** or **other nut butter**, how much did you usually eat?

- ☐ Less than 1 tablespoon
- ☐ 1 to 2 tablespoons
- ☐ More than 2 tablespoons

74. How often did you eat **roast beef** or **steak IN SANDWICHES**?

- ☐ NEVER (GO TO QUESTION 75)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 75 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months...**

74a. Each time you ate **roast beef** or **steak IN SANDWICHES**, how much did you usually eat?

- ☐ Less than 1 slice or less than 2 ounces
☐ 1 to 2 slices or 2 to 4 ounces
☐ More than 2 slices or more than 4 ounces

75. How often did you eat **turkey** or **chicken COLD CUTS** (such as loaf, luncheon meat, turkey ham, turkey salami, or turkey pastrami)? *(We will ask about other turkey or chicken later.)*

☐ NEVER (GO TO QUESTION 76)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

75a. Each time you ate **turkey** or **chicken COLD CUTS**, how much did you usually eat?

- ☐ Less than 1 slice
☐ 1 to 3 slices
☐ More than 3 slices

76. How often did you eat **luncheon** or **deli-style ham**? *(We will ask about other ham later.)*

☐ NEVER (GO TO QUESTION 77)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

76a. Each time you ate **luncheon** or **deli-style ham**, how much did you usually eat?

- ☐ Less than 1 slice
☐ 1 to 3 slices
☐ More than 3 slices

76b. How often was the luncheon or deli-style ham you ate **light, low-fat**, or **fat-free**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 77 appears in the next column

77. How often did you eat **other cold cuts** or **luncheon meats** (such as bologna, salami, corned beef, pastrami, or others, including low-fat)? *(Please do not include ham, turkey, or chicken cold cuts.)*

☐ NEVER (GO TO QUESTION 78)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

77a. Each time you ate **other cold cuts** or **luncheon meats**, how much did you usually eat?

- ☐ Less than 1 slice
☐ 1 to 3 slices
☐ More than 3 slices

77b. How often were the other cold cuts or luncheon meats you ate **light, low-fat**, or **fat-free**? *(Please do not include ham, turkey, or chicken cold cuts.)*

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

78. How often did you eat **canned tuna** (including in salads, sandwiches, or casseroles)?

☐ NEVER (GO TO QUESTION 79)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

78a. Each time you ate **canned tuna**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 2 ounces
☐ ¼ to ½ cup or 2 to 3 ounces
☐ More than ½ cup or more than 3 ounces

78b. How often was the canned tuna you ate **water-packed**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 79 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months**...

78c. How often was the canned tuna you ate **prepared with mayonnaise or other dressing** (including low-fat)?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

79. How often did you eat **GROUND chicken or turkey?** *(We will ask about other chicken and turkey later.)*

☐ NEVER (GO TO QUESTION 80)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

79a. Each time you ate **GROUND chicken or turkey**, how much did you usually eat?

- ☐ Less than 2 ounces or less than ½ cup
- ☐ 2 to 4 ounces or ½ to 1 cup
- ☐ More than 4 ounces or more than 1 cup

80. How often did you eat **beef hamburgers or cheeseburgers** from a **FAST FOOD** or **OTHER RESTAURANT**?

☐ NEVER (GO TO QUESTION 81)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

80a. Each time you ate **beef hamburgers or cheeseburgers** from a **FAST FOOD** or **OTHER RESTAURANT**, what size did you usually eat?

- ☐ Small hamburger (such as a regular Burger King or McDonald's Hamburger)
- ☐ Medium (such as McDonald's or Burger King Double Burger or Cheeseburger)
- ☐ Large (such as Burger King Whopper or Double Whopper or a McDonald's Double Quarter Pounder)

Question 81 appears in the next column

80b. Each time you ate **beef hamburgers or cheeseburgers** from a **FAST FOOD** or **OTHER RESTAURANT**, how much did you usually eat?

- ☐ Less than 1 burger
- ☐ 1 burger
- ☐ More than 1 burger

80c. How often did you have **cheeseburgers** rather than **hamburgers**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

81. How often did you eat **beef hamburgers or cheeseburgers** that were **NOT FROM A FAST FOOD** or **OTHER RESTAURANT**?

☐ NEVER (GO TO QUESTION 82)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

81a. Each time you ate **beef hamburgers or cheeseburgers** that were **NOT FROM A FAST FOOD** or **OTHER RESTAURANT**, how much did you usually eat?

- ☐ Less than 1 patty or less than 2 ounces
- ☐ 1 patty or 2 to 4 ounces
- ☐ More than 1 patty or more than 4 ounces

81b. How often were these beef hamburgers or cheeseburgers made with **lean ground beef**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

82. How often did you eat **ground beef in mixtures** (such as meatballs, casseroles, chili, or meatloaf)?

☐ NEVER (GO TO QUESTION 83)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 83 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months...**

82a. Each time you ate **ground beef in mixtures**, how much did you usually eat?

- ☐ Less than 3 ounces or less than ½ cup
☐ 3 to 8 ounces or ½ to 1 cup
☐ More than 8 ounces or more than 1 cup

83. How often did you eat **hot dogs** or **frankfurters**? *(Please do not include sausages or vegetarian hot dogs.)*

- ☐ NEVER (GO TO QUESTION 84)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

83a. Each time you ate **hot dogs** or **frankfurters**, how many did you usually eat?

- ☐ Less than 1 hot dog
☐ 1 to 2 hot dogs
☐ More than 2 hot dogs

83b. How often were the hot dogs or frankfurters you ate **light** or **low-fat**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

84. How often did you eat **beef mixtures** (such as beef stew, beef pot pie, beef and noodles, or beef and vegetables)?

- ☐ NEVER (GO TO QUESTION 85)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

84a. Each time you ate **beef mixtures**, how much did you usually eat?

- ☐ Less than 1 cup
☐ 1 to 2 cups
☐ More than 2 cups

Question 85 appears in the next column

85. How often did you eat **roast beef** or **pot roast**? *(Please do not include roast beef or pot roast in sandwiches.)*

- ☐ NEVER (GO TO QUESTION 86)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

85a. Each time you ate **roast beef** or **pot roast**, how much did you usually eat?

- ☐ Less than 2 ounces
☐ 2 to 5 ounces
☐ More than 5 ounces

86. How often did you eat **steak** (beef)? *(Please do not include steak in sandwiches)*

- ☐ NEVER (GO TO QUESTION 87)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

86a. Each time you ate **steak** (beef), how much did you usually eat?

- ☐ Less than 3 ounces
☐ 3 to 7 ounces
☐ More than 7 ounces

86b. How often was the steak you ate **lean** **steak**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

87. How often did you eat **pork** or **beef spareribs**?

- ☐ NEVER (GO TO QUESTION 88)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 88 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

87a. Each time you ate **pork** or **beef spareribs**, how much did you usually eat?

- ☐ Less than 4 ribs
☐ 4 to 12 ribs
☐ More than 12 ribs

88. How often did you eat **roast turkey, turkey cutlets, or turkey nuggets** (including in sandwiches)?

☐ NEVER (GO TO QUESTION 89)

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

88a. Each time you ate **roast turkey, turkey cutlets, or turkey nuggets**, how much did you usually eat? (Please note: 4 to 8 turkey nuggets = 3 ounces.)

- ☐ Less than 2 ounces
☐ 2 to 4 ounces
☐ More than 4 ounces

89. How often did you eat **chicken mixtures** (such as salads, sandwiches, casseroles, stews, or other mixtures)?

☐ NEVER (GO TO QUESTION 90)

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

89a. Each time you ate **chicken mixtures**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1½ cups
☐ More than 1½ cups

Question 90 appears in the next column

90. How often did you eat **baked, broiled, roasted, stewed, or fried chicken** (including nuggets)? (Please do not include chicken in mixtures.)

☐ NEVER (GO TO QUESTION 91)

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

90a. Each time you ate **baked, broiled, roasted, stewed, or fried chicken** (including nuggets), how much did you usually eat?

- ☐ Less than 2 drumsticks or wings, less than 1 breast or thigh, or less than 4 nuggets
☐ 2 drumsticks or wings, 1 breast or thigh, or 4 to 8 nuggets
☐ More than 2 drumsticks or wings, more than 1 breast or thigh, or more than 8 nuggets

90b. How often was the chicken you ate **fried chicken** (including deep fried) or **chicken nuggets**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

90c. How often was the chicken you ate **WHITE meat**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

90d. How often did you eat chicken **WITH skin**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

91. How often did you eat **baked ham or ham steak**?

☐ NEVER (GO TO QUESTION 92)

- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 92 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months**...

91a. Each time you ate **baked ham** or **ham steak**, how much did you usually eat?

- ☐ Less than 1 ounce
☐ 1 to 3 ounces
☐ More than 3 ounces

92. How often did you eat **pork** (including chops, roasts, and in mixed dishes)? *(Please do not include ham, ham steak, or sausage.)*

- ☐ NEVER (GO TO QUESTION 93)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

92a. Each time you ate **pork**, how much did you usually eat?

- ☐ Less than 2 ounces or less than 1 chop
☐ 2 to 5 ounces or 1 chop
☐ More than 5 ounces or more than 1 chop

93. How often did you eat **gravy** on meat, chicken, potatoes, rice, etc.?

- ☐ NEVER (GO TO QUESTION 94)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

93a. Each time you ate **gravy** on meat, chicken, potatoes, rice, etc., how much did you usually eat?

- ☐ Less than $\frac{1}{8}$ cup
☐ $\frac{1}{8}$ to $\frac{1}{4}$ cup
☐ More than $\frac{1}{4}$ cup

94. How often did you eat **liver** (all kinds) or **liverwurst**?

- ☐ NEVER (GO TO QUESTION 95)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 95 appears in the next column

94a. Each time you ate **liver** or **liverwurst**, how much did you usually eat?

- ☐ Less than 1 ounce
☐ 1 to 4 ounces
☐ More than 4 ounces

95. How often did you eat **bacon** (including low-fat)?

- ☐ NEVER (GO TO QUESTION 96)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

95a. Each time you ate **bacon**, how much did you usually eat?

- ☐ Fewer than 2 slices
☐ 2 to 3 slices
☐ More than 3 slices

95b. How often was the bacon you ate **light, low-fat, or lean**?

- ☐ Almost never or never
☐ About $\frac{1}{4}$ of the time
☐ About $\frac{1}{2}$ of the time
☐ About $\frac{3}{4}$ of the time
☐ Almost always or always

96. How often did you eat **sausage** (including low-fat)?

- ☐ NEVER (GO TO QUESTION 97)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

96a. Each time you ate **sausage**, how much did you usually eat?

- ☐ Less than 1 patty or 2 links
☐ 1 to 3 patties or 2 to 5 links
☐ More than 3 patties or 5 links

96b. How often was the sausage you ate **light, low-fat, or lean**?

- ☐ Almost never or never
☐ About $\frac{1}{4}$ of the time
☐ About $\frac{1}{2}$ of the time
☐ About $\frac{3}{4}$ of the time
☐ Almost always or always

Question 97 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

97. How often did you eat **fried shellfish** (such as crab, lobster, shrimp)?

- ☐ NEVER (GO TO QUESTION 98)
- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

97a. Each time you ate **fried shellfish**, how much did you usually eat?

- ☐ Less than 2 ounces
☐ 2 to 4 ounces
☐ More than 4 ounces

98. How often did you eat **shellfish** (such as crab, lobster, shrimp) **that was NOT FRIED**?

- ☐ NEVER (GO TO QUESTION 99)
- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

98a. Each time you ate **shellfish that was NOT FRIED**, how much did you usually eat?

- ☐ Less than 1 ounce
☐ 1 to 4 ounces
☐ More than 4 ounces

99. How often did you eat **salmon, fresh tuna or trout**?

- ☐ NEVER (GO TO QUESTION 100)
- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

99a. Each time you ate **salmon, fresh tuna or trout**, how much did you usually eat?

- ☐ Less than 2 ounces
☐ 2 to 6 ounces
☐ More than 6 ounces

Question 100 appears in the next column

100. How often did you eat **fish sticks** or other **fried fish** (not including shellfish)?

- ☐ NEVER (GO TO QUESTION 101)
- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

100a. Each time you ate **fish sticks** or other **fried fish**, how much did you usually eat?

- ☐ Less than 2 ounces or less than 1 fillet
☐ 2 to 7 ounces or 1 fillet
☐ More than 7 ounces or more than 1 fillet

101. How often did you eat **other fish that was NOT FRIED** (not including shellfish)?

- ☐ NEVER (GO TO INTRODUCTION TO QUESTION 102)
- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

101a. Each time you ate **other fish that was NOT FRIED**, how much did you usually eat?

- ☐ Less than 2 ounces or less than 1 fillet
☐ 2 to 5 ounces or 1 fillet
☐ More than 5 ounces or more than 1 fillet

Now think about all the meat, poultry, and fish you ate in the past 12 months and how they were prepared.

102. How often was **oil, butter, margarine, or other fat** used to **FRY, SAUTE, BASTE, OR MARINATE** any meat, poultry, or fish you ate? *(Please do not include deep frying.)*

- ☐ NEVER (GO TO QUESTION 103)
- | | |
|--|--|
| <input type="checkbox"/> 1-6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7-11 times per year | <input type="checkbox"/> 3-4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5-6 times per week |
| <input type="checkbox"/> 2-3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 103 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

102a. Which of the following **fats** were regularly used to prepare your meat, poultry, or fish?
(Mark all that apply.)

- | | |
|--|--|
| <input type="checkbox"/> Margarine (including low-fat) | <input type="checkbox"/> Corn oil |
| <input type="checkbox"/> Butter (including low-fat) | <input type="checkbox"/> Canola or rapeseed oil |
| <input type="checkbox"/> Lard, fatback, or bacon fat | <input type="checkbox"/> Oil spray (such as Pam or others) |
| <input type="checkbox"/> Olive oil | <input type="checkbox"/> Other kinds of oils |
| | <input type="checkbox"/> None of the above |

103. How often did you eat **tofu, soy burgers, or soy meat-substitutes**?

- ☐ NEVER (GO TO QUESTION 104)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

103a. Each time you ate **tofu, soy burgers, or soy meat-substitutes**, how much did you usually eat?

- ☐ Less than ¼ cup or less than 2 ounces
☐ ¼ to ½ cup or 2 to 4 ounces
☐ More than ½ cup or more than 4 ounces

104. Over the past 12 months, did you eat **soups**?

- ☐ NO (GO TO QUESTION 105)
☐ YES

104a. How often did you eat **soup IN THE WINTER**?

- ☐ NEVER
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per winter | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per winter | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

104b. How often did you eat **soup DURING THE REST OF THE YEAR**?

- ☐ NEVER
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 105 appears in the next column

104c. Each time you ate **soup**, how much did you usually eat?

- ☐ Less than 1 cup
☐ 1 to 2 cups
☐ More than 2 cups

104d. How often were the soups you ate **bean soups**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

104e. How often were the soups you ate **cream soups** (including chowders)?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

104f. How often were the soups you ate **tomato or vegetable soups**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

104g. How often were the soups you ate **broth soups** (including chicken) **with or without noodles or rice**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

105. How often did you eat **pizza**?

- ☐ NEVER (GO TO QUESTION 106)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 106 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months**...

105a. Each time you ate **pizza**, how much did you usually eat?

- ☐ Less than 1 slice or less than 1 mini pizza
- ☐ 1 to 3 slices or 1 mini pizza
- ☐ More than 3 slices or more than 1 mini pizza

105b. How often did you eat pizza with **pepperoni, sausage, or other meat**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

106. How often did you eat **crackers**?

- ☐ NEVER (GO TO QUESTION 107)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

106a. Each time you ate **crackers**, how many did you usually eat?

- ☐ Fewer than 4 crackers
- ☐ 4 to 10 crackers
- ☐ More than 10 crackers

107. How often did you eat **corn bread or corn muffins**?

- ☐ NEVER (GO TO QUESTION 108)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

107a. Each time you ate **corn bread or corn muffins**, how much did you usually eat?

- ☐ Less than 1 piece or muffin
- ☐ 1 to 2 pieces or muffins
- ☐ More than 2 pieces or muffins

Question 108 appears in the next column

108. How often did you eat **biscuits**?

- ☐ NEVER (GO TO QUESTION 109)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

108a. Each time you ate **biscuits**, how many did you usually eat?

- ☐ Fewer than 1 biscuit
- ☐ 1 to 2 biscuits
- ☐ More than 2 biscuits

109. How often did you eat **potato chips** (including low-fat, fat-free, or low-salt)?

- ☐ NEVER (GO TO QUESTION 110)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

109a. Each time you ate **potato chips**, how much did you usually eat?

- ☐ Fewer than 10 chips or less than 1 cup
- ☐ 10 to 25 chips or 1 to 2 cups
- ☐ More than 25 chips or more than 2 cups

109b. How often were the potato chips you ate **fat-free**? (Please do not include reduced-fat chips.)

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

110. How often did you eat **corn chips or tortilla chips** (including low-fat, fat-free, or low-salt)?

- ☐ NEVER (GO TO QUESTION 111)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 111 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

110a. Each time you ate **corn chips**, how much did you usually eat?

- ☐ Fewer than 10 chips or less than 1 cup
- ☐ 10 to 25 chips or 1 to 1½ cups
- ☐ More than 25 chips or more than 1½ cups

110b. How often were the corn chips or tortilla chips you ate **fat-free**? (Please do not include reduced-fat chips.)

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

111. How often did you eat **popcorn** (including low-fat)?

- ☐ NEVER (GO TO QUESTION 112)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

111a. Each time you ate **popcorn**, how much did you usually eat?

- ☐ Less than 2 cups, popped
- ☐ 2 to 5 cups, popped
- ☐ More than 5 cups, popped

112. How often did you eat **pretzels**?

- ☐ NEVER (GO TO QUESTION 113)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

112a. Each time you ate **pretzels**, how many did you usually eat?

- ☐ Fewer than 5 average twists
- ☐ 5 to 20 average twists
- ☐ More than 20 average twists

Question 113 appears in the next column

113. How often did you eat **peanuts, walnuts, seeds, or other nuts**?

- ☐ NEVER (GO TO QUESTION 114)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

113a. Each time you ate **peanuts, walnuts, seeds, or other nuts**, how much did you usually eat?

- ☐ Less than ¼ cup
- ☐ ¼ to ½ cup
- ☐ More than ½ cup

114. How often did you eat **energy, high-protein, or breakfast bars** (such as Power Bars, Balance, Clif, or others)?

- ☐ NEVER (GO TO QUESTION 115)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

114a. Each time you ate **energy, high-protein, or breakfast bars**, how much did you usually eat?

- ☐ Less than 1 bar
- ☐ 1 bar
- ☐ More than 1 bar

115. How often did you eat **yogurt** (NOT including frozen yogurt)?

- ☐ NEVER (GO TO QUESTION 116)
- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

115a. Each time you ate **yogurt**, how much did you usually eat?

- ☐ Less than ½ cup or less than 1 container
- ☐ ½ to 1 cup or 1 container
- ☐ More than 1 cup or more than 1 container

Question 116 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months**...

115b. How often was the **yogurt** you ate **low-fat** or **fat-free**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

116. How often did you eat **cottage cheese** (including low-fat)?

☐ NEVER (GO TO QUESTION 117)

- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

116a. Each time you ate **cottage cheese**, how much did you usually eat?

- ☐ Less than ¼ cup
- ☐ ¼ to 1 cup
- ☐ More than 1 cup

117. How often did you eat **cheese** (including low-fat; including on cheeseburgers or in sandwiches or subs)?

☐ NEVER (GO TO QUESTION 118)

- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

117a. Each time you ate **cheese**, how much did you usually eat?

- ☐ Less than ½ ounce or less than 1 slice
- ☐ ½ to 1½ ounces or 1 slice
- ☐ More than 1½ ounces or more than 1 slice

117b. How often was the cheese you ate **low-fat** or **fat-free**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 118 appears in the next column

118. How often did you eat **frozen yogurt, sorbet, or ices** (including low-fat or fat-free)?

☐ NEVER (GO TO QUESTION 119)

- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

118a. Each time you ate **frozen yogurt, sorbet, or ices**, how much did you usually eat?

- ☐ Less than ½ cup or less than 1 scoop
- ☐ ½ to 1 cup or 1 to 2 scoops
- ☐ More than 1 cup or more than 2 scoops

119. How often did you eat **ice cream, ice cream bars, or sherbet** (including low-fat or fat-free)?

☐ NEVER (GO TO QUESTION 120)

- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

119a. Each time you ate **ice cream, ice cream bars, or sherbet**, how much did you usually eat?

- ☐ Less than ½ cup or less than 1 scoop
- ☐ ½ to 1½ cups or 1 to 2 scoops
- ☐ More than 1½ cups or more than 2 scoops

119b. How often was the ice cream you ate **light, low-fat, or fat-free ice cream** or **sherbet**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

120. How often did you eat **cake** (including low-fat or fat-free)?

☐ NEVER (GO TO QUESTION 121)

- ☐ 1–6 times per year
- ☐ 7–11 times per year
- ☐ 1 time per month
- ☐ 2–3 times per month
- ☐ 1 time per week
- ☐ 2 times per week
- ☐ 3–4 times per week
- ☐ 5–6 times per week
- ☐ 1 time per day
- ☐ 2 or more times per day

Question 121 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

120a. Each time you ate **cake**, how much did you usually eat?

- ☐ Less than 1 medium piece
☐ 1 medium piece
☐ More than 1 medium piece

121. How often did you eat **cookies** or **brownies** (including low-fat or fat-free)?

- ☐ NEVER (GO TO QUESTION 122)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

121a. Each time you ate **cookies** or **brownies**, how much did you usually eat?

- ☐ Less than 2 cookies or 1 small brownie
☐ 2 to 4 cookies or 1 medium brownie
☐ More than 4 cookies or 1 large brownie

122. How often did you eat **doughnuts**, **sweet rolls**, **Danish**, or **pop-tarts**?

- ☐ NEVER (GO TO QUESTION 123)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

122a. Each time you ate **doughnuts**, **sweet rolls**, **Danish**, or **pop-tarts**, how much did you usually eat?

- ☐ Less than 1 piece
☐ 1 to 2 pieces
☐ More than 2 pieces

123. How often did you eat **sweet muffins** or **dessert breads** (including low-fat or fat-free)?

- ☐ NEVER (GO TO QUESTION 124)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

Question 124 appears in the next column

123a. Each time you ate **sweet muffins** or **dessert breads**, how much did you usually eat?

- ☐ Less than 1 medium piece
☐ 1 medium piece
☐ More than 1 medium piece

124. How often did you eat **fruit crisp**, **cobbler**, or **strudel**?

- ☐ NEVER (GO TO QUESTION 125)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

124a. Each time you ate **fruit crisp**, **cobbler**, or **strudel**, how much did you usually eat?

- ☐ Less than ½ cup
☐ ½ to 1 cup
☐ More than 1 cup

125. How often did you eat **pie**?

- ☐ NEVER (GO TO QUESTION 126)
- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

125a. Each time you ate **pie**, how much did you usually eat?

- ☐ Less than ¼ of a pie
☐ About ¼ of a pie
☐ More than ¼ of a pie

The next four questions ask about the kinds of pie you ate. Please read all four questions before answering.

125b. How often were the pies you ate **fruit pie** (such as apple, blueberry, others)?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 126 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

125c. How often were the pies you ate **cream, pudding, custard, or meringue pie**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

125d. How often were the pies you ate **pumpkin or sweet potato pie**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

125e. How often were the pies you ate **pecan pie**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

126. How often did you eat **chocolate candy**?

- ☐ NEVER (GO TO QUESTION 127)
- ☐ 1–6 times per year ☐ 2 times per week
- ☐ 7–11 times per year ☐ 3–4 times per week
- ☐ 1 time per month ☐ 5–6 times per week
- ☐ 2–3 times per month ☐ 1 time per day
- ☐ 1 time per week ☐ 2 or more times per day

126a. Each time you ate **chocolate candy**, how much did you usually eat?

- ☐ Less than 1 average bar or less than 1 ounce
- ☐ 1 average bar or 1 to 2 ounces
- ☐ More than 1 average bar or more than 2 ounces

127. How often did you eat **other candy**?

- ☐ NEVER (GO TO QUESTION 128)
- ☐ 1–6 times per year ☐ 2 times per week
- ☐ 7–11 times per year ☐ 3–4 times per week
- ☐ 1 time per month ☐ 5–6 times per week
- ☐ 2–3 times per month ☐ 1 time per day
- ☐ 1 time per week ☐ 2 or more times per day

127a. Each time you ate **other candy**, how much did you usually eat?

- ☐ Fewer than 2 pieces
- ☐ 2 to 9 pieces
- ☐ More than 9 pieces

Question 128 appears in the next column

128. How often did you eat **eggs, egg whites, or egg substitutes** (NOT counting eggs in baked goods and desserts)? *(Please include eggs in salads, quiche, and soufflés.)*

- ☐ NEVER (GO TO QUESTION 129)
- ☐ 1–6 times per year ☐ 2 times per week
- ☐ 7–11 times per year ☐ 3–4 times per week
- ☐ 1 time per month ☐ 5–6 times per week
- ☐ 2–3 times per month ☐ 1 time per day
- ☐ 1 time per week ☐ 2 or more times per day

128a. Each time you ate **eggs**, how many did you usually eat?

- ☐ 1 egg
- ☐ 2 eggs
- ☐ 3 or more eggs

128b. How often were the eggs you ate **egg substitutes or egg whites only**?

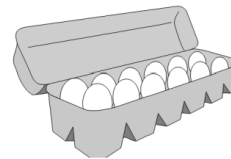
- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

128c. How often were the eggs you ate **regular whole eggs**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

128d. How often were the eggs you ate **cooked in oil, butter, or margarine**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always



Question 129 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

128e. How often were the eggs you ate part of **egg salad**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

129. How many cups of **coffee**, caffeinated or decaffeinated, did you drink (including coffee drinks such as Latte, Mocha, Frappuccino, etc.)?

☐ NONE (GO TO QUESTION 130)

- | | |
|--|---|
| <input type="checkbox"/> Less than 1 cup per month | <input type="checkbox"/> 5–6 cups per week |
| <input type="checkbox"/> 1–3 cups per month | <input type="checkbox"/> 1 cup per day |
| <input type="checkbox"/> 1 cup per week | <input type="checkbox"/> 2–3 cups per day |
| <input type="checkbox"/> 2–4 cups per week | <input type="checkbox"/> 4–5 cups per day |
| | <input type="checkbox"/> 6 or more cups per day |

129a. How often was the coffee you drank **decaffeinated**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

130. How many glasses, cans, or bottles of **COLD** or **ICED tea**, caffeinated or decaffeinated, did you drink?

☐ NONE (GO TO QUESTION 131)

- | | |
|---|---|
| <input type="checkbox"/> Less than 1 glass, can or bottle per month | <input type="checkbox"/> 5–6 glasses, cans or bottles per week |
| <input type="checkbox"/> 1–3 glasses, cans or bottles per month | <input type="checkbox"/> 1 glass, can or bottle per day |
| <input type="checkbox"/> 1 glass, can or bottle per week | <input type="checkbox"/> 2–3 glasses, cans or bottles per day |
| <input type="checkbox"/> 2–4 glasses, cans or bottles per week | <input type="checkbox"/> 4–5 glasses, cans or bottles per day |
| | <input type="checkbox"/> 6 or more glasses, cans or bottles per day |

130a. How often was the cold or iced tea you drank **decaffeinated** or **herbal**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 131 appears in the next column

130b. How often was the cold or iced tea you drank **presweetened with either sugar or artificial sweeteners** (such as Splenda, Equal, Sweet'N Low or others)?

- ☐ Almost never or never (GO TO QUESTION 131)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

130c. What kind of **sweetener** was added to your presweetened cold or iced tea most of the time?

- ☐ Sugar or honey
- ☐ Artificial sweeteners (such as Splenda, Equal, Sweet'N Low or others)

131. How many cups of **HOT tea**, caffeinated or decaffeinated, did you drink?

☐ NONE (GO TO QUESTION 132)

- | | |
|--|---|
| <input type="checkbox"/> Less than 1 cup per month | <input type="checkbox"/> 5–6 cups per week |
| <input type="checkbox"/> 1–3 cups per month | <input type="checkbox"/> 1 cup per day |
| <input type="checkbox"/> 1 cup per week | <input type="checkbox"/> 2–3 cups per day |
| <input type="checkbox"/> 2–4 cups per week | <input type="checkbox"/> 4–5 cups per day |
| | <input type="checkbox"/> 6 or more cups per day |

131a. How often was the hot tea you drank **decaffeinated** or **herbal**?

- ☐ Almost never or never
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

132. Over the past 12 months, did you add **sugar, honey or other sweeteners** to your tea or coffee (hot or iced)?

☐ NO (GO TO QUESTION 133)

☐ YES

132a. How often did you add **sugar** or **honey** to your coffee or tea (hot or iced)?

- ☐ Almost never or never (GO TO QUESTION 132c)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 132c appears on the next page
Question 133 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

132b. Each time **sugar** or **honey** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

132c. How often did you add **artificial sweetener** (such as Splenda, Equal, Sweet'N Low or others) to your coffee or tea?

- ☐ Almost never or never (GO TO QUESTION 133)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

132d. What kind of **artificial sweetener** did you usually use?

- ☐ Equal or aspartame
- ☐ Sweet'N Low or saccharin
- ☐ Splenda or sucralose
- ☐ Herbal extracts or other kind

132e. Each time **artificial sweetener** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 packet or less than 1 teaspoon
- ☐ 1 packet or 1 teaspoon
- ☐ More than 1 packet or more than 1 teaspoon

133. Over the past 12 months, did you add **whiteners** (such as cream, milk, or non-dairy creamer) to your tea or coffee?

☐ NO (GO TO QUESTION 134)

☐ YES

133a. How often was **non-dairy creamer** added to your coffee or tea?

- ☐ Almost never or never (GO TO QUESTION 133d)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

Question 133d appears in the next column

Question 134 appears on the next page

133b. Each time **non-dairy creamer** was added to your coffee or tea, how much was usually used?

- ☐ Less than 1 teaspoon
- ☐ 1 to 3 teaspoons
- ☐ More than 3 teaspoons

133c. What kind of **non-dairy creamer** did you usually use?

- ☐ Regular powdered
- ☐ Low-fat or fat-free powdered
- ☐ Regular liquid
- ☐ Low-fat or fat-free liquid

133d. How often was **cream** or **half and half** added to your coffee or tea?

- ☐ Almost never or never (GO TO QUESTION 133f)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

133e. Each time **cream** or **half and half** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 2 tablespoons
- ☐ More than 2 tablespoons

133f. How often was **milk** added to your coffee or tea?

- ☐ Almost never or never (GO TO QUESTION 134)
- ☐ About ¼ of the time
- ☐ About ½ of the time
- ☐ About ¾ of the time
- ☐ Almost always or always

133g. Each time **milk** was added to your coffee or tea, how much was usually added?

- ☐ Less than 1 tablespoon
- ☐ 1 to 3 tablespoons
- ☐ More than 3 tablespoons

133h. What kind of **milk** was usually added to your coffee or tea?

- ☐ Whole milk
- ☐ 2% milk
- ☐ 1% milk
- ☐ Skim, nonfat, or ½% milk
- ☐ Evaporated or condensed (canned) milk
- ☐ Soy milk
- ☐ Rice milk
- ☐ Other

Question 134 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

134. How often was **sugar** or **honey** added to foods you ate? (Please do not include sugar in coffee, tea, other beverages, or baked goods.)

☐ NEVER (GO TO INTRODUCTION TO QUESTION 135)

- | | |
|--|--|
| <input type="checkbox"/> 1–6 times per year | <input type="checkbox"/> 2 times per week |
| <input type="checkbox"/> 7–11 times per year | <input type="checkbox"/> 3–4 times per week |
| <input type="checkbox"/> 1 time per month | <input type="checkbox"/> 5–6 times per week |
| <input type="checkbox"/> 2–3 times per month | <input type="checkbox"/> 1 time per day |
| <input type="checkbox"/> 1 time per week | <input type="checkbox"/> 2 or more times per day |

134a. Each time **sugar** or **honey** was added to foods you ate, how much was usually added?

- ☐ Less than 1 teaspoon
☐ 1 to 3 teaspoons
☐ More than 3 teaspoons

The following questions are about the kinds of margarine, mayonnaise, sour cream, cream cheese, and salad dressing that you ate. If possible, please check the labels of these foods to help you answer.

135. Over the past 12 months, did you eat **margarine**?

☐ NO (GO TO QUESTION 136)

☐ YES

135a. How often was the margarine you ate **light**, **low-fat**, or **fat-free** (stick or tub)?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

136. Over the past 12 months, did you eat **butter**?

☐ NO (GO TO QUESTION 137)

☐ YES

136a. How often was the butter you ate **light** or **low-fat**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 137 appears in the next column

137. Over the past 12 months, did you eat **mayonnaise** or **mayonnaise-type dressing**?

☐ NO (GO TO QUESTION 138)

☐ YES

137a. How often was the mayonnaise you ate **light**, **low-fat** or **fat-free**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

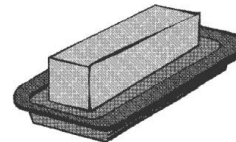
138. Over the past 12 months, did you eat **sour cream**?

☐ NO (GO TO QUESTION 139)

☐ YES

138a. How often was the sour cream you ate **light**, **low-fat**, or **fat-free**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always



139. Over the past 12 months, did you eat **cream cheese**?

☐ NO (GO TO QUESTION 140)

☐ YES

139a. How often was the cream cheese you ate **light**, **low-fat**, or **fat-free**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

Question 140 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

140. Over the past 12 months, did you eat **salad dressing**?

☐ NO (GO TO INTRODUCTION TO QUESTION 141)

☐ YES

140a. How often was the salad dressing you ate **light, low-fat or fat-free**?

- ☐ Almost never or never
☐ About ¼ of the time
☐ About ½ of the time
☐ About ¾ of the time
☐ Almost always or always

The following two questions ask you to summarize your usual intake of vegetables and fruits. Please do not include salads, potatoes, or juices.

141. Over the past 12 months, how many servings of **vegetables** (not including salad or potatoes) did you eat per week or per day?

- | | |
|---|--|
| <input type="checkbox"/> Less than 1 per week | <input type="checkbox"/> 2 per day |
| <input type="checkbox"/> 1–2 per week | <input type="checkbox"/> 3 per day |
| <input type="checkbox"/> 3–4 per week | <input type="checkbox"/> 4 per day |
| <input type="checkbox"/> 5–6 per week | <input type="checkbox"/> 5 or more per day |
| <input type="checkbox"/> 1 per day | |

142. Over the past 12 months, how many servings of **fruit** (not including juices) did you eat per week or per day?

- | | |
|---|--|
| <input type="checkbox"/> Less than 1 per week | <input type="checkbox"/> 2 per day |
| <input type="checkbox"/> 1–2 per week | <input type="checkbox"/> 3 per day |
| <input type="checkbox"/> 3–4 per week | <input type="checkbox"/> 4 per day |
| <input type="checkbox"/> 5–6 per week | <input type="checkbox"/> 5 or more per day |
| <input type="checkbox"/> 1 per day | |

143. Over the past month, which of the following foods did you eat **AT LEAST THREE TIMES?** (Mark all that apply.)

- | | |
|---|---|
| <input type="checkbox"/> Avocado, guacamole | <input type="checkbox"/> Olives |
| <input type="checkbox"/> Cheesecake | <input type="checkbox"/> Oysters |
| <input type="checkbox"/> Chocolate, fudge, or butterscotch toppings or syrups | <input type="checkbox"/> Pickles or pickled vegetables or fruit |
| <input type="checkbox"/> Chow mein noodles | <input type="checkbox"/> Plantains |
| <input type="checkbox"/> Croissants | <input type="checkbox"/> Pork neck bones, hock, head, feet |
| <input type="checkbox"/> Dried apricots | <input type="checkbox"/> Pudding or custard |
| <input type="checkbox"/> Egg rolls | <input type="checkbox"/> Veal, venison, lamb |
| <input type="checkbox"/> Granola bars | <input type="checkbox"/> Whipped cream, regular |
| <input type="checkbox"/> Hot peppers | <input type="checkbox"/> Whipped cream, substitute |
| <input type="checkbox"/> Jell-O, gelatin | |
| <input type="checkbox"/> Mangoes | |
| <input type="checkbox"/> Milkshakes or ice-cream sodas | <input type="checkbox"/> NONE |

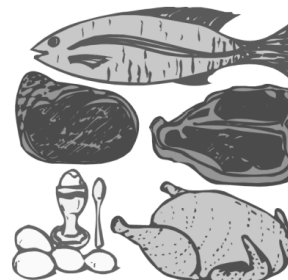
144. For **ALL** of the past 12 months, have you followed any type of **vegetarian diet**?

☐ NO (GO TO INTRODUCTION TO QUESTION 145)

☐ YES

144a. Which of the following foods did you **TOTALLY EXCLUDE** from your diet? (Mark all that apply.)

- ☐ Meat (beef, pork, lamb, etc.)
☐ Poultry (chicken, turkey, duck)
☐ Fish and seafood
☐ Eggs
☐ Dairy products (milk, cheese, etc.)



Introduction to Question 145 appears on the next page

This is a sample form. Do not use for scanning.

The next questions are about your use of vitamin pills or other supplements.

145. Over the past 12 months, did you take any **multivitamins**, such as One-a-Day-, Theragran-, Centrum-, or Prenatal-type multivitamins (as pills, liquids, or packets)?

☐ NO (GO TO INTRODUCTION TO QUESTION 147)

☐ YES

146. How often did you take **One-a-day-, Theragran-, Centrum- or Prenatal-type** multivitamins?

- ☐ Less than 1 day per month
- ☐ 1-3 days per month
- ☐ 1-3 days per week
- ☐ 4-6 days per week
- ☐ Every day

146a. Did your **multivitamin** usually contain **minerals** (such as iron, zinc, etc.)?

- ☐ NO
- ☐ YES
- ☐ Don't know

146b. For how many years have you taken **multivitamins**?

- ☐ Less than 1 year
- ☐ 1-4 years
- ☐ 5-9 years
- ☐ 10 or more years

146c. Over the past 12 months, did you take any **vitamins, minerals, or other herbal supplements** other than your multivitamin?

☐ NO

Thank you very much for completing this questionnaire! Because we want to be able to use all the information you have provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you:

- **Did not skip any pages and**
- **Crossed out the incorrect answer and circled the correct answer if you made any changes.**

☐ YES (GO TO INTRODUCTION TO QUESTION 147)

Introduction to Question 147 appears in the next column

These last questions are about the vitamins, minerals, or herbal supplements you took that are **NOT** part of a One-a-day-, Theragran-, or Centrum-type of multivitamin.

Over the past 12 months...

147. How often did you take **Antacids such as Tums or Rolaids**?

☐ NEVER (GO TO QUESTION 148)

- ☐ Less than 1 day per month
- ☐ 1-3 days per month
- ☐ 1-3 days per week
- ☐ 4-6 days per week
- ☐ Every day

147a. When you took **Antacids such as Tums or Rolaids**, about how many tablets or lozenges did you take in one day?

- ☐ Less than 1
- ☐ 1
- ☐ 2
- ☐ 3
- ☐ 4 or more
- ☐ Don't know

147b. Was your antacid usually "extra strength"?

- ☐ NO
- ☐ YES
- ☐ Don't know

147c. For how many years have you taken **Antacids such as Tums or Rolaids**?

- ☐ Less than 1 year
- ☐ 1-4 years
- ☐ 5-9 years
- ☐ 10 or more years

148. How often did you take **Calcium** (with or without Vitamin D) (**NOT** as part of a multivitamin in Question 146 or antacid in Question 147)?

☐ NEVER (GO TO QUESTION 149)

- ☐ Less than 1 day per month
- ☐ 1-3 days per month
- ☐ 1-3 days per week
- ☐ 4-6 days per week
- ☐ Every day

Question 149 appears on the next page

This is a sample form. Do not use for scanning.

Over the **past 12 months...**

148a. When you took **Calcium**, about how much elemental calcium did you take in one day?
(If possible, please check the label for elemental calcium.)

- ☐ Less than 500 mg
- ☐ 500–599 mg
- ☐ 600–999 mg
- ☐ 1,000 mg or more
- ☐ Don't know

148b. Did your **Calcium** usually contain **Vitamin D**?

- ☐ NO
- ☐ YES
- ☐ Don't know

148c. Did your **Calcium** usually contain **Magnesium**?

- ☐ NO
- ☐ YES
- ☐ Don't know

148d. Did your **Calcium** usually contain **Zinc**?

- ☐ NO
- ☐ YES
- ☐ Don't know

148e. For how many years have you taken **Calcium**?

- ☐ Less than 1 year
- ☐ 1–4 years
- ☐ 5–9 years
- ☐ 10 or more years

149. How often did you take **Iron** (**NOT** as part of a multivitamin in Question 146)?

☐ NEVER (GO TO QUESTION 150)

- ☐ Less than 1 day per month
- ☐ 1–3 days per month
- ☐ 1–3 days per week
- ☐ 4–6 days per week
- ☐ Every day

149a. For how many years have you taken **Iron**?

- ☐ Less than 1 year
- ☐ 1–4 years
- ☐ 5–9 years
- ☐ 10 or more years

Question 150 appears in the next column

150. How often did you take **Vitamin C** (**NOT** as part of a multivitamin in Question 146)?

☐ NEVER (GO TO QUESTION 151)

- ☐ Less than 1 day per month
- ☐ 1–3 days per month
- ☐ 1–3 days per week
- ☐ 4–6 days per week
- ☐ Every day

150a. When you took **Vitamin C**, about how much did you take in one day?

- ☐ Less than 500 mg
- ☐ 500–999 mg
- ☐ 1,000–1,499 mg
- ☐ 1,500–1,999 mg
- ☐ 2,000 mg or more
- ☐ Don't know

150b. For how many years have you taken **Vitamin C**?

- ☐ Less than 1 year
- ☐ 1–4 years
- ☐ 5–9 years
- ☐ 10 or more years

151. How often did you take **Vitamin E** (**NOT** as part of a multivitamin in Question 146)?

☐ NEVER (GO TO INTRODUCTION TO QUESTION 152)

- ☐ Less than 1 day per month
- ☐ 1–3 days per month
- ☐ 1–3 days per week
- ☐ 4–6 days per week
- ☐ Every day

151a. When you took **Vitamin E**, about how much did you take in one day?

- ☐ Less than 400 IU
- ☐ 400–799 IU
- ☐ 800–999 IU
- ☐ 1,000 IU or more
- ☐ Don't know

151b. For how many years have you taken **Vitamin E**?

- ☐ Less than 1 year
- ☐ 1–4 years
- ☐ 5–9 years
- ☐ 10 or more years

Introduction to Question 152 appears on the next page

This is a sample form. Do not use for scanning.

Over the past 12 months...

The last two questions ask you about other supplements you took more than once per week.

152. Please mark any of the following **single supplements** you took more than once per week (NOT as part of a multivitamin in Question 147):

- | | |
|--|---|
| <input type="checkbox"/> B-6 | <input type="checkbox"/> Occu-vite/Eye health |
| <input type="checkbox"/> B-complex | <input type="checkbox"/> Potassium |
| <input type="checkbox"/> B-12 | <input type="checkbox"/> Selenium |
| <input type="checkbox"/> Beta-carotene | <input type="checkbox"/> Vitamin A |
| <input type="checkbox"/> Folic acid/folate | <input type="checkbox"/> Vitamin D |
| <input type="checkbox"/> Magnesium | <input type="checkbox"/> Zinc |

153. Please mark any of the following **herbal, botanical, or other supplements** you took more than once per week.

- | | |
|---|--|
| <input type="checkbox"/> Chondroitin | <input type="checkbox"/> Ginseng |
| <input type="checkbox"/> Coenzyme Q-10 | <input type="checkbox"/> Glucosamine/
chondroitin |
| <input type="checkbox"/> Echinacea | <input type="checkbox"/> Peppermint |
| <input type="checkbox"/> Energy supplements | <input type="checkbox"/> Probiotics |
| <input type="checkbox"/> Fish oil/omega 3's | <input type="checkbox"/> Saw palmetto |
| <input type="checkbox"/> Flaxseed/oil | <input type="checkbox"/> Soy supplement |
| <input type="checkbox"/> Garlic | <input type="checkbox"/> Sports supplements |
| <input type="checkbox"/> Ginger | <input type="checkbox"/> St. John's wort |
| <input type="checkbox"/> Ginkgo biloba | <input type="checkbox"/> Other |

Thank you very much for completing this questionnaire! Because we want to be able to use all the information you have provided, we would greatly appreciate it if you would please take a moment to review each page making sure that you:

- Did not skip any pages and
- Crossed out the incorrect answer and circled the correct answer if you made any changes.

Appendix II: KDRAFT Consent Form

**Alzheimer's Disease Ketogenic Diet Retention and Feasibility Trial
Consent Form**

Principal Investigator: Debra Sullivan, PhD, RD

INTRODUCTION

You are being asked to join a research study. You are being asked to take part in this study because you have been diagnosed with Mild Cognitive Impairment or Alzheimer's Disease. You do not have to participate in this research study. The main purpose of research is to create new knowledge for the benefit of future patients and society in general. Research studies may or may not benefit the people who participate.

Research is voluntary, and you may change your mind at any time. There will be no penalty to you if you decide not to participate, or if you start the study and decide to stop early. Either way, you can still get medical care and services at the University of Kansas Medical Center (KUMC).

This consent form explains what you have to do if you are in the study. It also describes the possible risks and benefits. Please read the form carefully and ask as many questions as you need to, before deciding about this research.

You can ask questions now or anytime during the study. The researchers will tell you if they receive any new information that might cause you to change your mind about participating.

This research study will take place at the University of Kansas Medical Center (KUMC) with Debra Sullivan, PhD, RD as the researcher. About 15 people will be in the study at KUMC.

BACKGROUND

The brain requires a constant supply of energy in order to function properly. This energy is usually provided by sugar called glucose that is converted from the carbohydrates eaten in the diet. In Alzheimer's Disease, the brain may not properly use glucose as energy. There is another source of energy called ketones that can be used by the brain. In order for the body to change to ketones as the source of energy rather than glucose, the person must eat a very low carbohydrate diet. This diet relies on higher fat and protein intake while drastically decreasing carbohydrates eaten.

It is currently unknown whether patients with Alzheimer's Disease can maintain eating a very low carbohydrate diet for an extended period of time. This study intends to determine whether participants have the ability to eat a very low carbohydrate diet for 3 months and whether this diet provides benefit to participant memory and brain energy function.



PURPOSE

The purpose of this study is to determine whether participants have the ability to eat a very low carbohydrate diet for 3 months and whether this diet provides benefit to participant memory and brain energy function.

PROCEDURES

If you are eligible and you decide to participate in this study, your participation will last approximately 4 months. On the first visit, approximately 15 minutes of your time will be needed to take a blood sample. The amount of blood that will be taken can be up to a little more than 3 tablespoons. Afterward, approximately one more hour of your time will be required to take 2 memory tests so that we can evaluate memory status. Approximately one more hour of your time may be needed to take a body composition scan with a Dual Energy X-Ray Absorptiometry (DEXA) machine. After the DEXA scan, approximately 10 minutes of your time will be needed for an electrocardiogram (ECG). The initial visit may take up to 3 hours. On a second visit you will meet with a registered dietitian to receive education on how to eat a very low carbohydrate diet. The diet education may take up to 2 hours.

If you have been diagnosed with mild Alzheimer's disease, you will be asked to participate in an additional step on a different date. This step is a Magnetic Resonance Spectroscopy (MRS) scan. This will allow us to compare how the brain uses energy before and after eating a very low carbohydrate diet. MRS scans may take up to an hour of time.

You will be asked to eat a very low carbohydrate diet for the duration of 3 months. This diet may restrict carbohydrates that you eat to 20 grams per day or less. The registered dietitian will provide sufficient information to better understand how to maintain this diet. You will be provided easy-to-follow menus for your specific energy needs to help you know exactly which foods you should eat at each meal. At the end of each month that you have been on the diet, you will be required to return to the Clinical Research Center to meet with the dietitian, measure body weight, take an ECG (end of month 1 and 2) and provide another blood sample.

Ketostix instruction will be provided to help determine whether the food that you are eating allows you to use ketones for energy or not. This is a very quick process, taking only a few seconds of time, and only requires a small collection of urine. You will be asked to use these ketostix in the evening on a daily basis during the entire time that you are on the very low carbohydrate diet. If ketostix indicate that ketones are not being used for energy, we request that the dietitian be contacted immediately.

You will be asked to complete 3-day food records for each study visit. This 3-day food record should include two weekdays and one weekend day. The registered dietitian will instruct you how to complete the food record.

After the 3 months that you have eaten a very low carbohydrate diet, we once again request that you complete a blood draw, memory test and DEXA scan. Mild



Alzheimer's disease participants will be asked to participate in another MRS scan. You will also be asked to fill out a short questionnaire. This visit may take up to 4 hours of time.

At the end of 3 months, there will be a 1-month period in which the you will no longer be required to follow the very low carbohydrate diet. Once this month has ended, you will return to the KUMC Clinical Research Center to meet with the dietitian, complete another blood draw, and take a final set of memory tests. This visit may take a little more than 2 hours.

Description of Procedures

(1) Blood samples will be drawn:

- Blood pressure, pulse, and weight will be measured to make sure that the participant is healthy enough to have his or her blood drawn.
- You will be asked if you ever fainted, bled excessively, or had a bad response to having blood drawn.
- A needle will be used to take up to a little more than 3 tablespoons of blood from a vein in the arm. The blood will be taken to a research laboratory and assigned a number. Only the researchers on the study team will know that your blood came from you.

(2) DEXA scans will be taken:

- DEXA scans are very simple. All you need to do is relax while the machine scans your body.
- You will remain fully clothed but you will be asked to remove your shoes before lying down on a flat padded table.
- The procedure should not take long, but could take up to an hour of time.
- The DEXA scans will be used to measure body fat, lean tissue and bone density.

(3) ECG will be taken:

- An electrocardiogram (ECG) is a test that gives us a measure of the heart's electrical activity. You will be asked to lie flat on a table and several small electrode pads (like stickers) will be placed on the body. This test takes about 10 minutes.

(4) MRS scans may be taken:

- An MRS scan is a test that is done in a standard MRI machine.
- You will lie down in a comfortable position on a table.
- The table will move your body, head first, into an opening where the scanner is located. This scanner has a magnet that will produce the images needed for our study.
- You may hear a few "banging" noises during the study.
- If at any point you need to communicate with the person performing the scan, you will be able to do so with an alert bulb and speaker system.



- MRS scans require that you remain still during the scanning process and may take up to an hour of time.

(5) Information produced from the blood samples, DEXA and MRS will be saved in a research database:

- Information obtained from blood samples, DEXA and MRS may be used to prepare reports that describe what has been learned by this study. Identity will not be revealed. Other than the neurologist who referred you to this study and the study personnel, no one will know who participated in this study.
- Information obtained from the blood sample will be saved as long as this research project is active.
- If you are a KUMC patient and information that could influence your medical diagnosis or medical treatment is obtained during this study, then that information will be provided to the KUMC neurologist who referred you to this study.
- Neither you nor your family members will be given written or verbal reports of the research data.

RISK

The potential risks of participating in this study are as follows:

- The risks of having blood drawn include bruising and swelling in the area from which the blood is drawn. Drawing blood can also make someone feel nervous, sweaty, lightheaded, or even faint. We are taking steps to reduce the chance of something bad happening while blood is being drawn. You can also have us stop drawing blood at any time, even if we have not filled all the tubes we want to fill.
- As a research subject, you will be exposed to radiation in this study from DEXA scans. This radiation exposure is not needed for medical care and is intended for research only. You are exposed to radiation every day. This radiation comes from the sun and the earth. It is called background radiation. The amount of radiation from the DEXA scan is about the same amount that you receive in two days from background radiation. The risk from this radiation exposure is very low.
- The ECG may cause some redness or itching where the pads are placed.
- The effects of magnetic fields in an MRI scanner have been extensively studied, and there are no known significant risks with an MRI exam. You may, however, be bothered by feelings of confinement (claustrophobia), and by the noise made by the magnet during the procedure. You will be asked to wear earplugs or earphones while in the magnet. MRS scans require that you remain still during the scanning process and may take up to an hour of time. You may not



participate in this study if you have a pacemaker, an implanted defibrillator or certain other implanted electronic or metallic devices. It is important for you to advise the MRI staff if you have had brain surgery for a cerebral aneurysm, or if you have implanted medical or metallic devices, shrapnel, or other metal, such as metal in your eye.

- Some risks may be associated with a very low carbohydrate diet. These risks include potential weight loss, fatigue, or adverse reactions. If you experience any of these issues, contact the dietitian to discuss options of measures that can be taken to improve these problems.
- There is a risk of feeling uncomfortable while answering some of the questions in the questionnaire. If you feel uncomfortable at any time you may skip a question or stop participating all together.
- There may be other risks that are not yet known.

NEW FINDINGS STATEMENT

You will be informed if any significant new findings develop during the course of this study that may affect your willingness to continue participating in the study.

BENEFITS

There is a possibility that you will receive personal benefit from this study. Potential benefits could include improved memory and better brain function. There is also the potential that you may either experience no change in memory or continued memory decline. It is possible that this study could help us find new ways to treat Alzheimer's Disease.

ALTERNATIVES

Participation in this study is voluntary. Deciding not to participate will in no way affect the care or service that you receive at KUMC.

COSTS

We are unsure how a very low carbohydrate diet will affect grocery costs. It is possible that eating a very low carbohydrate diet could increase the amount of money spent on groceries. It is also possible that the very low carbohydrate diet could decrease the amount of money spent on groceries.

Travel costs can be expected with study as you will be asked to travel to the KUMC Clinical Research Center in Fairway, KS on several occasions.

PAYMENT TO SUBJECTS

Participants will be paid \$25 upon completion of each of the 5 visits for a total of \$125 to use toward travel expenses to the KUMC Clinical Research Center. Payment will be made by check. If you withdraw before the study is complete, you will be paid for each visit completed.



The KUMC Research Institute will be given your name, address, social security number, and the title of this study to allow them to write checks for your study payments. Study payments are taxable income. A Form 1099 will be sent to you and to the Internal Revenue Service if your payments are \$600 or more in a calendar year.

IN THE EVENT OF INJURY

In the event that you experience any problem during this study, you should immediately contact Dr. Sullivan at (913) 588-5357. If it is after 5:00 p.m., a holiday or a weekend, you should call (913) 481-7240 and ask to speak with Dr. Sullivan.

If you have a bodily injury as a result of participating in this study, treatment will be provided for you at the usual charge. Treatment may include first aid, emergency care and follow-up care, as needed. Claims will be submitted to your health insurance policy, your government program, or other third party, but you will be billed for the costs that are not covered by the insurance. You do not give up any legal rights by signing this form.

INSTITUTIONAL DISCLAIMER STATEMENT

If you think you have been harmed as a result of participating in research at the University of Kansas Medical Center (KUMC), you should contact the Director, Human Research Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160. Under certain conditions, Kansas state law or the Kansas Tort Claims Act may allow for payment to persons who are injured in research at KUMC.

CONFIDENTIALITY AND PRIVACY AUTHORIZATION

The researchers will protect your information, as required by law. Absolute confidentiality cannot be guaranteed because persons outside the study team may need to look at your study records. The researchers may publish the results of the study. If they do, they will only discuss group results. Your name will not be used in any publication or presentation about the study.

Your health information is protected by a federal privacy law called HIPAA. By signing this consent form, you are giving permission for KUMC to use and share your health information. If you decide not to sign the form, you cannot be in the study.

The researchers will only use and share information that is needed for the study. To do the study, they will collect health information from the study activities. You may be identified by information such as name, address, phone, date of birth, social security number, or other identifiers. Your health information will be used at KU Medical Center by Dr. Sullivan, members of the research team and KUMC Human Subjects Committee and other committees and offices that review and monitor research studies. Study records might be reviewed by government officials who oversee research, if a regulatory review takes place.



All study information that is sent outside KU Medical Center will have your name and other identifying characteristics removed, so that your identity will not be known. Because identifiers will be removed, your health information will not be re-disclosed by outside persons or groups and will not lose its federal privacy protection.

Dr. Sullivan and the research team may share information about you with persons or groups that are not part of the research team if that information is felt to be crucial to your medical management. Such persons or groups who receive such health information may not be required by law to protect it.

Your permission to use and share the health information will not expire unless you cancel it.

QUESTIONS

Before you sign this form, the member of the research team who is obtaining this consent should answer all your questions. You can talk to the researchers if you have any more questions, suggestions, concerns, or complaints after signing this form. If you have any questions about your rights as a research subject, or if you want to talk with someone who is not involved in the study, you may call the Human Subjects Committee at (913) 588-1240. You may also write the Human Subjects Committee at Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160.

SUBJECT RIGHTS AND WITHDRAWAL FROM THE STUDY

Your participation in this study is voluntary and the choice not to participate or to quit at any time can be made without penalty. Not participating or quitting will have no effect upon the medical care or treatment you receive now or in the future at the University of Kansas Medical center. The entire study may be discontinued for any reason without your consent by the investigator conducting the study.

You have a right to change your mind about allowing the research team to have access to your health information. If you want to cancel permission to use health information, you should send a written request to Dr. Sullivan. The mailing address is Debra K. Sullivan, PhD, RD, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160. If you cancel permission to use health information, you will be withdrawn from the study. The research team may use and share information that was gathered before they received your cancellation.



CONSENT

A member of the research team has given me information about this research study, explained what will be done and how long it will take, and explained any inconvenience, discomfort, or risk that may be experienced during this study.

I freely and voluntarily consent to participate in this research study. I have read and understand the information in this form and have had an opportunity to ask questions and have them answered. **I will be given a signed copy of the consent form to keep for my records.**

Participant's Signature

Date

Participant's Name (Print)

Signature of Person Obtaining Consent

Date

Print Name of Person Obtaining Consent

In the future, our research team will be conducting additional studies. Please initial the appropriate line to indicate whether or not you are willing to have us contact you when such future studies occur.

____ Yes, I am willing to be contacted about future studies for which I might be eligible.

____ No, I do not want to be contacted about future studies for which I might be eligible.

A separate consent would be obtained at the time of your participation in any additional studies.



STUDY PARTNER RESPONSIBILITIES AND CONSENT

As the study partner of the participant in this study, your responsibilities include assisting the participant in:

- following the very low carbohydrate diet
- daily ketostix testing
- arriving to KUMC facilities for study events
- contacting research team members for any questions or concerns

I freely and voluntarily consent to participating as a study partner in this research study. I have read and understand the information in this form and have had an opportunity to ask questions and have them answered.

Study Partners' s Signature

Date

Study Partner's Name (Print)

Signature of Person Obtaining Consent

Date

Print Name of Person Obtaining Consent



Appendix III: KDRAFT Surrogate Consent Form

CONSENT FOR SURROGATE DECISION MAKERS
Alzheimer's Disease Ketogenic Diet Retention and Feasibility Trial
Consent Form

Principal Investigator: Debra Sullivan, PhD, RD

INTRODUCTION

As a relative or other individual who is making decisions on behalf of a person diagnosed with Mild Cognitive Impairment or Alzheimer's Disease, you are being asked to approve his or her participation in a research study that looks at the ability to stay on a very low carbohydrate diet by patients with Alzheimer's Disease. It is called the Alzheimer's Disease Ketogenic Diet Retention and Feasibility Trial. This research study will be conducted at the University of Kansas Medical Center with Dr. Debra Sullivan, PhD, RD as the principal investigator. Approximately 15 subjects will be enrolled at KUMC.

The potential participant (the person for whom you are making decisions) does not have to participate in this research study. Participating in research is different from getting standard health care. The main purpose of research is to benefit future patients and society in general. Participants might get personal benefit from being in this study, but you should understand that the purpose of research is to create new knowledge.

BACKGROUND

The brain requires a constant supply of energy in order to function properly. This energy is usually provided by sugar called glucose that is converted from the carbohydrates eaten in the diet. In Alzheimer's Disease, the brain may not properly use glucose as energy. There is another source of energy called ketones that can be used by the brain. In order for the body to change to ketones as the source of energy rather than glucose, the person must eat a very low carbohydrate diet. This diet relies on higher fat and protein intake while drastically decreasing carbohydrates eaten.

It is currently unknown whether patients with Alzheimer's Disease can maintain eating a very low carbohydrate diet for an extended period of time. This study intends to determine whether participants have the ability to eat a very low carbohydrate diet for 3 months and whether this diet provides benefit to participant memory and brain energy function.

PURPOSE

The purpose of this study is to determine whether participants have the ability to eat a very low carbohydrate diet for 3 months and whether this diet provides benefit to participant memory and brain energy function.

PROCEDURES

If the potential participant is eligible and you decide for them to participate in this study, their participation will last approximately 4 months. On the first visit, approximately 15 minutes of time will be needed take a blood sample. The amount of blood that will be taken



can be up to a little more than 3 tablespoons. Afterward, approximately one hour of time will be required to take 2 memory tests so that we can evaluate memory status. Approximately one more hour of time will be needed to take a body composition scan with a Dual Energy X-Ray Absorptiometry (DEXA) machine. After the DEXA scan, approximately 10 minutes of time will be needed for an electrocardiogram (ECG). The initial visit may take up to 3 hours. On a second visit you will meet with a registered dietitian to receive education on how to prepare a very low carbohydrate diet for the person for which you are providing care. The diet education may take up to 2 hours.

If the person for whom you provide care has been diagnosed with mild Alzheimer's disease, that participant will be asked to participate in an additional step on a different date. This step is a Magnetic Resonance Spectroscopy (MRS) scan. This will allow us to compare how the brain uses energy before and after eating a very low carbohydrate diet. MRS scans may take up to an hour of time.

You will be asked to prepare the participant a very low carbohydrate diet for the duration of 3 months. This diet may restrict carbohydrates that the participant eats to 20 grams per day or less. The registered dietitian will provide sufficient information to better understand how to maintain this diet. You will be provided easy-to-follow menus for the participant's needs to help you know exactly which foods he or she should eat at each meal. At the end of each month that the participant has been on the diet, the participant will be required to return to the Clinical Research Center to meet with the dietitian, measure body weight, take an ECG (end of month 1 and 2) and provide another blood sample.

Ketostix instruction will be provided to help determine whether the food that the participant is eating allows them to use ketones for energy or not. This is a very quick process, taking only a few seconds of time, and only requires a small collection of urine. The participant will be asked to use these ketostix in the evening on a daily basis during the entire time that he or she is on the very low carbohydrate diet. If ketostix indicate that ketones are not being used for energy, we request that the dietitian be contacted immediately.

You will be asked to complete 3-day food records for the participant for each study visit. This 3-day food record should include two weekdays and one weekend day. The registered dietitian will instruct you how to complete the food record.

After the 3 months that the participant has eaten a very low carbohydrate diet, we will once again request that he or she complete another blood draw, memory test and DEXA scan. Mild Alzheimer's disease participants will be asked to participate in another MRS scan. The participant will also be asked to fill out a short questionnaire. This visit may take up to 4 hours of time.

At the end of 3 months, there will be a 1-month period in which the participant will no longer be required to follow the very low carbohydrate diet. Once this month has ended, the participant will return to the KUMC Clinical Research Center to meet with the dietitian,



complete another blood draw, and take a final set of memory tests. This visit may take a little more than 2 hours.

Description of Procedures

(1) Blood samples will be drawn:

- Blood pressure, pulse, and weight will be measured to make sure that the participant is healthy enough to have his or her blood drawn.
- The participant will be asked if he or she has ever fainted, bled excessively, or had a bad response to having blood drawn.
- A needle will be used to take up to a little more than 3 tablespoons of blood from a vein in the arm. The blood will be taken to a research laboratory and assigned a number. Only the researchers on the study team will know from which participant the blood sample came.

(2) DEXA scans will be taken:

- DEXA scans are very simple. All the participant needs to do is relax while the machine scan his or her body.
- The participant will remain fully clothed but will be asked to remove their shoes before lying down on a flat padded table.
- The procedure should not take long, but could take up to an hour of time.
- The DEXA scans will be used to measure body fat, lean tissue and bone density.

(3) ECG will be taken:

- An electrocardiogram (ECG) is a test that gives us a measure of the heart's electrical activity. You will be asked to lie flat on a table and several small electrode pads (like stickers) will be placed on the body. This test takes about 10 minutes.

(4) MRS scans may be taken:

- An MRS scan is a test that is done in a standard MRI machine.
- The participant will lie down in a comfortable position on a table.
- The table will move the participant's body, head first, into an opening where the scanner is located. This scanner has a magnet that will produce the images needed for our study.
- The participant may hear a few "banging" noises during the study.
- If at any point the participant needs to communicate with the person performing the scan, they will be able to do so with an alert bulb and speaker system.
- MRS scans require that the participant remain still during the scanning process and may take up to an hour of time.

(5) Information produced from the blood samples, DEXA and MRS will be saved in a research database:

- Information obtained from blood samples, DEXA and MRS may be used to prepare reports that describe what has been learned by this study. Identity will not be revealed. Other than the neurologist who referred you to this study and the study personnel, no one will know who participated in this study.



- Information obtained from the blood sample will be saved as long as this research project is active.
- If the participant is a KUMC patient and information that could influence his or her medical diagnosis or medical treatment is obtained during this study, then that information will be provided to the KUMC neurologist who referred you to this study.
- Neither the participant nor family members will be given written or verbal reports of the research data.

RISK

The potential risks of participating in this study are as follows:

- There is a small chance that something bad could happen while blood is being drawn. The risks of having blood drawn include bruising and swelling in the area from which the blood is drawn. Drawing blood can also make someone feel nervous, sweaty, lightheaded, or even faint. We are taking steps to reduce the chance of something bad happening to while blood is being drawn. The participant can also have us stop drawing blood at any time, even if we have not filled all the tubes we want to fill.
- As a research subject, the participant will be exposed to radiation in this study from DEXA scans. This radiation exposure is not needed for medical care and is intended for research only. The participant is exposed to radiation every day. This radiation comes from the sun and the earth. It is called background radiation. The amount of radiation from the DEXA scan is about the same amount that you receive in two days from background radiation. The risk from this radiation exposure is very low.
- The ECG may cause some redness or itching where the pads are placed.
- The effects of magnetic fields in an MRI scanner have been extensively studied, and there are no known significant risks with an MRI exam. The participant may, however, be bothered by feelings of confinement (claustrophobia), and by the noise made by the magnet during the procedure. The participant will be asked to wear earplugs or earphones while in the magnet. MRS scans require that the participant remain still during the scanning process and may take up to an hour of time. The participant may not participate in this study if he or she has a pacemaker, an implanted defibrillator or certain other implanted electronic or metallic devices. It is important for you to advise the MRI staff if the participant has had brain surgery for a cerebral aneurysm, or if he or she has implanted medical or metallic devices, shrapnel, or other metal, such as metal in his or her eye.
- Some risks may be associated with a very low carbohydrate diet. These risks include potential weight loss, fatigue, or adverse reactions. If the participant experiences any of these issues, contact the dietitian to discuss options of measures that can be taken to improve these problems.
- There may be other risks that are not yet known.



- There is a risk of feeling uncomfortable while answering some of the questions in the questionnaire. If you feel uncomfortable at any time you may skip a question or stop participating all together.

NEW FINDINGS STATEMENT

You will be informed if any significant new findings develop during the course of this study that may affect your willingness to allow the participant to continue participating in the study.

BENEFITS

There is a possibility that the participant will receive personal benefit from this study. Potential benefits could include improved memory and better brain function. There is also the potential that the participant may either experience no change in memory or continued memory decline. It is possible that this study could help us find new ways to treat Alzheimer's Disease.

ALTERNATIVES

Participation in this study is voluntary. Deciding not to participate will in no way affect the care or service that the person for whom you provide care will receive at KUMC.

COSTS

We are unsure how a very low carbohydrate diet will affect grocery costs. It is possible that eating a very low carbohydrate diet could increase the amount of money spent on groceries. It is also possible that the very low carbohydrate diet could decrease the amount of money spent on groceries.

Travel costs can be expected with study as the participant will be asked to travel to the KUMC Clinical Research Center in Fairway, KS on several occasions.

PAYMENT TO SUBJECTS

Participants will be paid \$25 upon completion of each of the 5 visits for a total of \$125 to use toward travel expenses to the KUMC Clinical Research Center. Payment will be made by check. If the participant withdraws before the study is complete, he will be paid for each visit completed.

The KUMC Research Institute will be given your name, address, social security number, and the title of this study to allow them to write checks for your study payments. Study payments are taxable income. A Form 1099 will be sent to you and to the Internal Revenue Service if your payments are \$600 or more in a calendar year.

IN THE EVENT OF INJURY

In the event that the participant experiences any problem during this study, you should immediately contact Dr. Sullivan at (913) 588-5357. If it is after 5:00 p.m., a holiday or a weekend, you should call (913) 481-7240 and ask to speak with Dr. Sullivan.



If the participant has a bodily injury as a result of participating in this study, treatment will be provided to him or her at the usual charge. Treatment may include first aid, emergency care and follow-up care, as needed. Claims will be submitted to the participant's health insurance policy, government program, or other third party, but the participant will be billed for the costs that are not covered by the insurance. You do not give up any legal rights by signing this form.

INSTITUTIONAL DISCLAIMER STATEMENT

If you think the participant has been harmed as a result of participating in research at the University of Kansas Medical Center (KUMC), you should contact the Director, Human Research Protection Program, Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160. Under certain conditions, Kansas state law or the Kansas Tort Claims Act may allow for payment to persons who are injured in research at KUMC.

CONFIDENTIALITY AND PRIVACY AUTHORIZATION

Study records that identify research participants will be kept confidential as required by law. Researchers cannot guarantee absolute confidentiality. Efforts will be made to keep the participant's personal information confidential. If the results of this study are published or presented in public, information that identifies participants will be removed.

The privacy of health information is protected by a federal law known as the Health Insurance Portability and Accountability Act (HIPAA). By signing this consent form, you are giving permission ("authorization") for KUMC to use and share health information about the participant for purposes of this research study. If you decide not to sign the form, the person for whom you are making decisions cannot be in the study.

To do this research, the research team needs to collect health information that identifies participants. The information may include items such as name, address, phone, date of birth, social security number or other identifiers. The research team will collect information from study activities described in the Procedures section of this form and information from the medical record that relates to study participation. The health information will be used at KUMC by Dr. Sullivan, members of the research team, The University of Kansas Hospital Medical Record Department, the KUMC Research Institute and officials at KUMC who oversee research, including members of the KUMC Human Subjects Committee and other committees and offices that review and monitor research studies.

All study information that is sent outside KU Medical Center will have the participant's name and other identifying characteristics removed, so that his or her identity will not be known. Because identifiers will be removed, the participant's health information will not be re-disclosed by outside persons or groups and will not lose its federal privacy protection.



Dr. Sullivan and the research team may share information about the participant with persons or groups that are not part of the research team if that information is felt to be crucial to the participant's medical management. Such persons or groups who receive such health information may not be required by law to protect it.

Your permission to use and share the participant's health information will not expire unless you or the participant cancels it. Any research information that is placed in the medical record will be kept indefinitely.

During the study, participants will have access to any study information that is placed in their KUMC medical record. However, some research-specific information is kept only by the researcher. Access to all of the research-specific information may not be available until the end of the study.

QUESTIONS

Before you sign this form, the member of the research team who is obtaining this consent should answer all your questions. You can talk to the researchers if you have any more questions, suggestions, concerns, or complaints after signing this form. If you have any questions about the participant's rights as a research subject, or if you want to talk with someone who is not involved in the study, you may call the Human Subjects Committee at (913) 588-1240. You may also write the Human Subjects Committee at Mail Stop #1032, University of Kansas Medical Center, 3901 Rainbow Blvd, Kansas City, KS 66160.

SUBJECT RIGHTS AND WITHDRAWAL FROM THE STUDY

The participant's participation in this study is voluntary and that the choice not to participate or to quit at any time can be made without penalty. Not participating or quitting will have no effect upon the medical care or treatment the participant receives now or in the future at the University of Kansas Medical Center. The entire study may be discontinued for any reason without your consent by the investigator conducting the study.

You have a right to change your mind about allowing the research team to have access to the participant's health information. If you want to cancel permission to use health information, you should send a written request to Dr. Sullivan. The mailing address is Debra Sullivan, PhD, RD, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160. If you cancel permission to use health information, the participant will be withdrawn from the study. You can also request that the research team no longer use the participant's blood sample or materials derived from the blood sample. If so, the participant's blood sample or materials derived from the blood sample will be destroyed. The research team may use and share information that was gathered before they received your cancellation.



CONSENT

A member of the research team has given me information about this research study, explained what will be done and how long it will take, and explained any inconvenience, discomfort, or risk that may be experienced during this study.

On behalf of the person for whom you are making decisions, you freely and voluntarily consent to participate in this research study. You have read and understand the information in this form and have had an opportunity to ask questions and have them answered. **I will be given a signed copy of the consent form to keep for my records.**

As a legal guardian or representative, I, _____,
Print Guardian Name
authorize the participation of _____ in this research study.
Print Participant Name

I understand that I may not authorize participation in this study if the individual has previously expressed wishes to the contrary, either orally or in writing.

I am (please initial one of the following categories) :

_____ *Legal guardian or Durable Power of Attorney for Healthcare Decisions*
_____ *Adult or emancipated minor's spouse (unless legally separated)*
_____ *Adult child*
_____ *Parent*
_____ *Adult relative by blood or marriage*

Signature of Legal Guardian/Representative

Time Date

Print Name of Legal Guardian/Representative

Signature of Person Obtaining Consent

Time Date

Print Name of Person Obtaining Consent

In the future, our research team will be conducting additional studies. Please initial the appropriate line to indicate whether or not you are willing to have us contact you on behalf of the participant when such future studies occur.

___ Yes, I am willing to be contacted about future studies for which the participant might be eligible.

___ No, I do not want to be contacted about future studies for which the participant might be eligible.

A separate consent would be obtained at the time of participant's participation in any additional studies.



ASSENT

I am a person with a neurologic disorder. I have seen this Consent form for the Surrogate Decision Makers and understand that I am agreeing to participate in a research project. I have been given the opportunity to ask any questions that I might have about my participation and by signing on the line below indicate my willingness to participate. I understand that I may withdraw my assent and stop participating at any time.

Signature of Participant

Time

Date

Print Name of Participant

Signature of Legal Guardian/Representative

Time

Date

Print Name of Legal Guardian/Representative

Signature of Person Obtaining Consent

Time

Date

Print Name of Person Obtaining Consent



STUDY PARTNER RESPONSIBILITIES AND CONSENT

As the study partner of the participant in this study, your responsibilities include assisting the participant in:

- following the very low carbohydrate diet
- daily ketostix testing
- arriving to KUMC facilities for study events
- contacting research team members for any questions or concerns

I freely and voluntarily consent to participating as a study partner in this research study. I have read and understand the information in this form and have had an opportunity to ask questions and have them answered.

Study Partners' s Signature

Date

Study Partner's Name (Print)

Signature of Person Obtaining Consent

Date

Print Name of Person Obtaining Consent



Appendix IV: Ketogenic Diet Education Materials

Ketogenic Diet Education



The University of Kansas

Alzheimer's Disease Center
&
Department of Dietetics and Nutrition

Alzheimer's Disease Ketogenic Diet Retention and Feasibility Trial

The Ketogenic Diet

Introduction

The Ketogenic Diet is a high fat, very low carbohydrate diet that might be beneficial in Alzheimer's disease.

It is important to understand the basic goals of the ketogenic diet. The body normally uses glucose that comes from carbohydrate (i.e. bread, sugar, potatoes, etc.) as its main source for energy. The goal of the ketogenic diet is to switch the body's main fuel source from glucose to fat. This is done by increasing the intake of fats and greatly reducing the intake of carbohydrates. Eating more than the amount of carbohydrate prescribed by the dietitian can cause the diet to fail.

But isn't fat bad for you?

In recent years, foods considered "low fat" have been believed to be the healthiest option; however, understanding fat is much more complex than this. Fat is a very important nutrient. It is necessary for many normal, healthy processes in the body. It is true that too much fat is unhealthy, but the amount of fat consumed in the ketogenic diet has not been shown to be harmful.

Ketogenic Diet Rules

- Prepare only the foods that are specified in the ketogenic diet. No substitutions.
- Weigh all foods according to prescribed meals.
- Eat every morsel of food at each meal within 30 minutes.
- Use a small spatula to clean every drop of fat from dishes and cups.
- Space meals 3-4 hours apart to hunger between meals.
- Drink all of the recommended fluids. Drink Liberally.
- Take the prescribed vitamin and mineral supplements every day.

What is a person allowed to eat on the Ketogenic Diet diet?

The ketogenic diet is a precisely prescribed diet that contains foods and drinks that are high in fat and low in carbohydrate. Fat produces more calories per gram than carbohydrate or protein; therefore, the amount of food prepared for each ketogenic diet meal may seem like a small amount of food.

A registered dietitian, who is familiar with the diet, will calculate the amount of calories, fat, carbohydrate and protein and create prescribed individualized menus. The dietitian will attempt to design the menus to resemble the types of foods the participant normally eats and likes. This is not completely possible in all cases, especially if the participant's favorite foods are usually high in carbohydrates.

The ketogenic diet alone is deficient in calcium and certain vitamins. Participants will be prescribed a calcium and vitamin supplement that they will need to take during the time that they are on the ketogenic diet. It is also important that participants on the ketogenic diet drink lots of water to stay hydrated and help prevent unwanted side effects like nausea and constipation.

Ketogenic Monitoring Guidelines

- Check and record urine ketones daily.
- Attend regularly scheduled Ketogenic Diet appointments with study dietitian.

The participant or guardians have the right to request discontinuation of the diet at any time during the course of treatment.

Are there any side effects to the Ketogenic Diet?

Potential side effects to the ketogenic diet include:

1. Constipation: This is seen in most people that begin the diet. There are ways to improve the problem, so it should not be a reason to discontinue the diet.
2. Nausea and vomiting: Dehydration may cause nausea, lack of appetite and vomiting. This is why it is important to drink plenty of fluids, mainly water. Treatment involves re-hydration. If the problem continues, contact the study dietitian. The dietitian may need to adjust the diet.
3. Hypoglycemia: The participant will be taught the symptoms of hypoglycemia. If hypoglycemia occurs, contact the study dietitian.
4. Hypercholesterolemia: Most people on the ketogenic diet experience decreased cholesterol levels; however, there is potential for the diet to raise cholesterol levels. We will check cholesterol levels to monitor any changes.
5. Pancreatitis: The pancreas is an organ located in the back of the abdomen near the kidneys. The pancreas' primary responsibility is to break down fat. In some people, the pancreas can't handle the increased fat of the ketogenic diet. In these instances, the pancreas becomes swollen. The person experiences severe abdominal discomfort and the abdomen is very tender to touch. Vomiting often occurs. In this situation, the person needs to be seen by a physician immediately for diagnosis and treatment.

Fats

- Medium Chain Triglyceride Oil (MCT Oil)
 - Medium chain triglycerides (MCT) are very beneficial for the Ketogenic diet since they produce ketones better than other oils.
- Grade A Butter
- Coconut Oil
 - Coconut oil has the highest concentration of medium chain triglycerides of all foods.
- Margarine or Soy Margarine
- Vegetable Oils
 - Canola
 - Flax (limited amount)
 - Olive
 - Soy
 - Walnut
 - Sunflower
 - Sesame
- Mayonnaise – Hellmann’s has the least carbohydrate
- Sour Cream



- Coconut Milk
- Avocado
- Nuts
 - Almonds
 - Macadamia Nuts
 - Pecans
 - Flax Seeds
- Flours
 - Keep flours refrigerated!
 - Coconut flour
 - Almond flour

Other Ideas:

- Mix mayonnaise with a small amount of cream. Add a pinch of dill weed and salt (free foods) to make a salad dressing.
- Mix mayonnaise into chopped meats such as chicken, turkey or pork.
- Make egg salad or tuna salad with mayonnaise.
- Stir a small amount of soy sauce, hot sauce, catsup into Mayo to change flavor and color.
- Blend oil into mayonnaise. Mix into finely chopped chicken, turkey or tuna.
- Blend some or all of the oil into cream.

"Other Ideas" courtesy Children's Mercy Hospital – Kansas City

Cream



36% Cream	40% Cream
Serving size: 1/2 fl. Oz	Serving size: 1/2 fl. Oz
Calories: 50	Calories: 60
Calories from fat: 50	Calories from fat: 55
Total Fat: 5g	Total Fat: 6g
Total Carbohydrate: 0 (or 1g)	Total Carbohydrate: 0 (or 1g)
Protein: 0g	Protein: 0g

**Most cream from the grocery store is 36% cream*

Use only the amount of cream allotted on your meal. For recipes with whipped cream, weigh the cream after it has been whipped.

Tips:

- Mix with water to make milk
- Mix with 5 drops of pure vanilla or chocolate extract. Mix this mixture with water or diet club soda.
- Make a “cream soda” by mixing the cream with diet sodas such as root beer.
- Mix whipped cream and a few drops of pure extract and sweetener. Eat with spoon.
- Freeze whipped cream; flavor with pure extract and allowed sweetener.
- Mix whipped cream with allotted fruit (chopped). Eat with a spoon.
- Make “hot chocolate” by adding unsweetened baking chocolate (must be calculated). Heat until warm.
- Make Eggnog with cream (from a calculated recipe). Eggnog can be microwaved or frozen.
- Add sour cream to whipped cream (from a calculated recipe). Add chopped fruit. Tastes like yogurt.

Drinking is best!

- Make cream soups
- Make sauces
- Whip
- Freeze
- Ice cream, creamcicles

Adapted from material from Children’s Mercy Hospital – Kansas City

Fruit

- Use fresh or frozen
- Unsweetened Fruit
- Unsweetened Juice
- Do not use dried or dehydrated fruit

How to Weigh:

- The weights of the lower carbohydrate fruits (10%) are used in menus.
- If you want the 15% fruit, use 2/3 of the amount in grams for the 10% fruit.



Best Choice:

10% Fruit

- Applesauce
- Apricot
- Blackberry
- Cantaloupe
- Grapefruit (pink, red, white)
- Guava
- Honeydew melon
- Kiwi
- Mango
- Nectarine
- Orange
- Papaya
- Peaches
- Pineapple
- Strawberries
- Tangerine
- Watermelon

15% Fruit

- Apple with skin
- Blueberries
- Cherries (sweet or sour)
- Grapes
- Pears
- Plums



Adapted from KetoCalculator

Vegetables

Preparation

- Either: fresh, frozen or canned
- Boil, steam, grill, bake or microwave
- Drain the vegetables after cooking and before weighing



Group A

If you use group A vegetables, you can use twice the amount as what is listed in the menu.

Asparagus
Beet greens
Cabbage
Celery
Chicory
Cucumbers
Eggplant
Endive
Green pepper
Poke – cooked

Radish
Rhubarb
Sauerkraut
Summer squash
Swiss chard
Tomato – raw
Tomato juice
Turnips – cooked
Turnip greens – cooked
Watercress

Group B

If you use group B vegetables, use the amount listed in the menu.

Beets – cooked
Broccoli – cooked
Brussels sprouts
Carrots – raw or cooked
Cauliflower – raw or cooked
Dandelion greens – cooked
Green beans
Kale – cooked

Kohlrabi – cooked
Mushrooms – raw
Mustard greens
Okra – cooked
Onion – raw or cooked
Rutabaga – cooked
Tomato – cooked
Winter squash - cooked

Adapted from KetoCalculator

Ketogenic Ingredients

Protein

These are just suggestions: family and individual tastes can be taken into account. Check with the dietitian.



All protein should be weighed after cooking.

Animal Protein—*All items can be fresh or frozen*

- Eggs
- Chicken
- Turkey
- Pork
- Lamb
- Beef
- Game Meat: duck, goat, deer

Dairy

Choose Full Fat Options

Always choose the least processed options. Whole block cheese is preferred over pre-grated to avoid anti-clumping agents.

- Cream 36%, 40%
- Cream Cheese
- Sour Cream
- Yogurt
- Cottage Cheese
- Buttermilk
- Cheese
- Cheddar
- Mozzarella
- Provolone
- Parmesan
- Swiss
- Blue

Seafood Protein—*All items can be fresh or frozen*

- Bass
- Catfish
- Cod
- Halibut
- Mahi-Mahi
- Salmon
- Tilapia
- Tuna
- Clams
- Crab
- Crawfish
- Lobster
- Shrimp
- Scallops

Baking

Baking Ingredients

- Coconut flour
- Shredded coconut – unsweetened
- Almond flour/meal
- Hazelnut flour
- Psyllium husk
- Baking powder
- Baking soda
- Bickford's flavoring

Miscellaneous

- Nori
- Almond milk – unsweetened
- Soy milk – unsweetened
- Tahini paste
- Tofu
- Tempeh
- Decaffeinated tea
- Gelatin, unflavored
- Broth: chicken, beef, vegetable

Sweeteners

- Liquid stevia
- Powdered stevia
- Saccharine
- Sucralose

Herbs

- Dried varieties should be calculated into a meal if it is more than a pinch.
- Fresh and whole varieties may be steeped to infuse flavors, but must be removed prior to eating.



Adapted from material from Children's Mercy Hospital – Kansas City

Special Occasions

Holidays can still be enjoyed while on the ketogenic diet. Contact the study dietitian ahead of time to help you plan your special occasion menu.

Phone: (913) 945-7664
Email: mtaylor3@kumc.edu

Ketogenic Birthday Cake



Thanksgiving Dinner

Turkey with Gravy
Green Bean Casserole
Mashed Cauliflower
Crustless Pumpkin Pie

Recipe sources:
www.ketocook.com
www.myketocal.com
www.ketocuisine.com



Processed Foods

** All items in this section should be used in limited quantities at the discretion of your dietitian. Nutritional contents will vary significantly between brands.

- Turkey
- Ham
- Pepperoni
- Bologna
- Salami
- Cheese – American
- Italian sausage
- Breakfast sausage
- Bacon
- Hot dogs
- Canned or potted meats
- Miracle and Shiratake Noodles
- Walden Farm's product
- Just the Cheese Products
- Low carb bread, tortilla



Adapted from material from Children's Mercy Hospital – Kansas City

Quick Ketogenic Diet Grocery List

*Orange indicates food with some carbohydrate. Eat these items in moderation.

*Red indicates food higher in carbohydrate. Eat these items sparingly.

Meat/Protein

- Bacon
- Steak
- Ground Beef
- Eggs
- Ribs (pork or beef)
- Roast (pork or beef)
- Pork loins, chops, or steaks
- Chicken (breast, thighs, wings)
- Ham
- Sausage
- Deli cold cuts
- Pepperoni
- Salami
- Prosciutto

Seafood

- Shrimp
- Tilapia
- Cod
- Scallops
- Crab
- Tuna
- Albacore
- Salmon

Dairy

- Cheese
- Heavy Cream
- Sour Cream
- Butter
- Cream Cheese

Vegetables

- Avocado
- Bell peppers
- Mushrooms
- Cucumbers
- Cabbage
- Cauliflower
- Romaine lettuce
- Broccoli
- Artichoke hearts
- Kale
- Asparagus
- Spinach
- Bok Choy
- Garlic
- Onion

Fruit

- Blueberries
- Raspberries
- Blackberries
- Strawberries
- Cranberries

Nuts/Seeds

- Almonds
- Hazelnuts
- Macadamias
- Pistachios
- Walnuts
- Pecans
- Sesame
- Sunflower
- Pumpkin
- Flax

Condiments/Dressings

- Mayonnaise
- Mustard
- Soy sauce
- Hot sauce
- Ranch
- Salsa
- Lemon juice
- Lime juice

Other/Miscellaneous

- Unsweetened cocoa powder
- Unsweetened almond milk
- Nut butters
- Flax Meal
- Almond Meal/Almond Flour
- Olives
- Pickles
- Herbs
- Spices
- Coconut oil
- Olive oil
- Pork rinds
- Beef jerky

High carb foods – should be avoided on a ketogenic diet:

- **Sugars** and sweetened foods: read labels and avoid any foods which contain brown sugar, powdered sugar, cane sugar, corn syrup, sorghum, honey, maple syrup, sucrose, maltose, fructose, glucose, lactose, and the sugar alcohols such as sorbitol, xylitol, mannitol and maltitol.
- **Grain and Grain Products** (wheat, barley, rye, sorghum, tricale, teff, spelt, rice, etc..) and products made from grain flours: bread, waffles, pancakes, pasta, muffins, cold cereals, hot cereals, bread crumbs, tortillas, crackers, cookies, cakes, pies, pretzels, etc.
- **Corn** products, including cornbread, tamale wrappers, corn chips, grits, polenta, popcorn and cornmeal.
- **Potatoes** and other starchy tubers such as sweet potatoes and potato products such as hash browns, potato chips, tater tots, etc.
- **Starchy vegetables**, such as corn, sweet potatoes, lima beans, peas, okra, and artichokes.
- **Canned soups and stews**, as most canned products contain hidden starchy thickeners.
- **Boxed processed foods**, because most are high in wheat and sugar.
- **Fruit** (dried, fresh, frozen): Fruit is high in carbs. Berries are the lowest in carbohydrate, so if you have to have something sweet, you could eat 1 or 2 strawberries on a ketogenic diet, but the fructose might halt ketosis.
- **Beans and lentils**, which are high in starch.
- **Beers**, as they are made from grain (there are low carb beers, but since you only have so many carbs per day, you have to decide if you want to spend them on beer.)
- **Dessert wines** such as Icewine, Beerenauslese, Trockenbeerenauslese, Ruster Ausbruch, Moscato, Riesling. These are high in sugar.
- **Regular sodas**: Sweetened soda pop or soft drinks are very high in sugar.
- **Juices made from fruit and vegetables**. These can be high in sugar.
- **Milk**, especially skim and 1%. Milk contains lactose, a type of sugar.

Sample Ketogenic Menu

Day #1	Day #2
<u>Breakfast</u>	<u>Breakfast</u>
2 eggs	3 slices of bacon
3 slices of bacon	Veggie Scramble
<i>*Cook eggs in oil from bacon</i>	<i>*Sauté peppers and onions in oil from bacon</i>
1 cup sautéed spinach	<i>*Scramble 2 eggs into peppers and onions in skillet</i>
Coffee – add 2 tbsp of heavy cream	Coffee – add 2 tbsp of heavy cream
1 tbsp MCT Oil	1 tbsp MCT Oil
<u>Lunch</u>	<u>Lunch</u>
3 oz. chicken breast strips	Tuna Salad
<i>*Pan cooked in 2 tbsp olive oil</i>	<i>*Mix tuna with Hellman's mayonnaise, chopped celery and a small amount of grapes</i>
2-3 cups mixed greens	Roasted Brussels sprouts
1 celery stalk	<i>*Cut Brussels sprouts in half, toss in 2 tbsp olive oil – roast on baking sheet 350 deg. For 25 minutes</i>
¼ cup Italian salad dressing	
<u>Dinner</u>	<u>Dinner</u>
Bacon Cheeseburger Soup – recipe included	4 oz. baked ham
½ cup steamed broccoli w/ butter	1 cup summer squash, sautéed in olive oil
1 tbsp MCT Oil	1 cup salad greens, olive oil and vinegar as dressing
<u>Dessert</u>	<i>*Add sliced avocado to salad</i>
Low Carb Vanilla Ice Cream	1 tbsp MCT Oil
<i>*Freeze whipped cream, flavor with pure vanilla extract and sweetener (Stevia or Truvia).</i>	

Appendix V: KDRAFT Data Collection

NAME: _____ ID #: _____

ASSESSMENT PERIOD:

BASELINE
1 MONTH
2 MONTHS
3 MONTHS
4 MONTHS

INTERVIEWED _____
ENTERED _____
CHECKED _____
RD CHECKED _____

KDRAFT: 3-DAY FOOD RECORD

INSTRUCTIONS:

- Using the forms provided, please write down ALL of the foods you eat and beverages you drink on the following 3 consecutive days:

DAY 1

DAY 2

DAY 3

Note: 3 consecutive days must include 2 weekdays and 1 weekend day. For example, Thursday/Friday/Saturday or Sunday/Monday/Tuesday

- Write down ALL of the foods you eat and beverages you drink each day, including soda, water, coffee, and even small bites of food and snacks between meals.
- Write down AS MANY DETAILS AS YOU CAN about the foods and beverages you ate in the appropriate columns (see example below):
 - ✓ **MEAL:** What would you call the meal or snack – breakfast, snack, lunch, brunch, dinner, etc.?
 - ✓ **TIME:** When did you eat or drink each food or beverage?
 - ✓ **LOCATION:** Where did you eat or drink each food or beverage?
 - ✓ **FOOD/BEVERAGE:** What did you eat or drink?
 - ✓ **AMOUNT:** How much of each food and beverage did you consume?
 - ✓ **CALORIES:** How many calories are there in the foods and beverages you consumed? Refer to the Nutrition Facts labels for this info!
 - ✓ **OTHER DETAILS:** What is the brand name? What else does it say on the label – fat free, low fat, regular, etc.? How was the food prepared? Did you add anything to the food before eating it?
- Please list one item per line and write legibly.

MEAL	TIME	LOCATION	FOOD/BEVERAGE	AMOUNT	CALORIES		OTHER DETAILS
					(IF KNOWN)		
Break	7:00am	Home	Scrambled Eggs	2	140		large, scrambled, no fat added
			Bacon	3 slices	210		thick cut, pan fried
			Avocado	1/2			California
			Whole Milk	8 fl. oz.	150		
Snack	10:30am	Work	Almonds	23	160		Blue Diamond, Raw Natural
			Water	16.9 fl. oz.	0		Dasani, bottled

[illegible]

Please list all vitamin, mineral, and herbal supplements you took today.

Type/Brand of Supplement	Reason for Taking	Amount Taken (dosage)	Frequency of Dose (times/day)
<i>Example: One A Day Brand Multi-Vitamin for Women</i>	<i>General Health</i>	<i>1 Tablet</i>	<i>Once per day</i>
<i>Example: Fish Oil - CVS Brand</i>	<i>Lower Triglycerides</i>	<i>1 softgel (1200mg)</i>	<i>3 softgels per day</i>

- Would you consider your intake of foods and beverages today to be typical of most days or was it considerably more or less? Explain why if not typical: _____
- Would you consider this food record to be complete and match what you really ate this day or are there any missing meals, snacks or beverages? Explain why if not complete and accurate: _____

[illegible]

[illegible]

Week #1
In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #2
In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #3
In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #4
In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #5
In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #6
In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #7
In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #8
In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #9
In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #10
In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #11

In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Week #12

In which range was your Ketostix result?

Day #1	Day #2	Day #3	Day #4	Day #5	Day #6	Day #7
___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___	___/___/___
<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large	<input type="checkbox"/> Negative <input type="checkbox"/> Trace <input type="checkbox"/> Small <input type="checkbox"/> Moderate <input type="checkbox"/> Large

Screening

Participant ID _____
Date _____
(MM-DD-YYYY)

Participant Demographic Information

First Name _____
Middle Initial _____
(Just the initial)
Last Name _____
Street Address _____
City _____
State _____
Zip Code _____
Preferred Phone _____
(Include Area Code (000-000-0000))
Alternate Phone _____
(Include Area Code (000-000-0000))
E-mail _____
Date of Birth _____
(MM-DD-YYYY)
Age _____
Gender
☐ Female
☐ Male
Race
☐ White
☐ Black or African American
☐ American Indian or Alaska Native
☐ Asian
☐ Hispanic or Latino
☐ Other (specify) _____
☐ Decline
If race is one that is not listed in the preceding question, specify what the race is. You do not have to report this information if you do not wish to do so.
Is the potential participant a member of the KUMC Alzheimer's Disease Center Registry?
☐ No
☐ Yes

Study Partner Information

First Name	<input type="text"/>
Last Name	<input type="text"/>
Study Partner Relationship to Participant	<input type="radio"/> son <input type="radio"/> daughter <input type="radio"/> wife <input type="radio"/> husband <input type="radio"/> friend <input type="radio"/> other
Street Address	<input type="text"/>
City	<input type="text"/>
State	<input type="text"/>
Zip Code	<input type="text"/>
Preferred Phone	<input type="text"/> (Include Area Code (000-000-0000))
Alternate Phone	<input type="text"/> (Include Area Code (000-000-0000))
E-mail	<input type="text"/>

The next several questions are about the health of the participant.

Clinical Cognitive Diagnosis	<input type="radio"/> Mild Cognitive Impairment (CDR 0.5) <input type="radio"/> Mild Alzheimer's Disease (CDR 0.5 - 1.0) <input type="radio"/> Moderate Alzheimer's Disease (CDR 2.0)
Does the potential participant consume greater than 2 drinks of alcohol per day?	<input type="radio"/> No <input type="radio"/> Yes
Has the potential participant had a MRI or CT scan of the head or brain?	<input type="radio"/> No <input type="radio"/> Yes
Does the potential participant have cochlear, dental, or other implants that would prevent having an MRI of the head?	<input type="radio"/> No <input type="radio"/> Yes
Does the potential participant have history of diabetes?	<input type="radio"/> No <input type="radio"/> Yes
Is the potential participant insulin dependent?	<input type="radio"/> No <input type="radio"/> Yes
Does the potential participant have history of cancer?	<input type="radio"/> No <input type="radio"/> Yes
If yes to history of cancer, how recently?	<input type="text"/> (MM-YYYY)
Does the potential participant have a pacemaker?	<input type="radio"/> No <input type="radio"/> Yes

Does the potential participant have history of heart attack, heart disease, any arrhythmia, or heart surgery such as a bypass or stent placement?

- ☐ No
☐ Yes

If yes to history of heart attack, heart disease, any arrhythmia, or heart surgery such as a bypass or stent placement, how recently?

(MM-YYYY)

Does the potential participant have history of stroke, ministroke, or TIA?

- ☐ No
☐ Yes

If yes to history of stroke, ministroke, or TIA, how recently?

(MM-YYYY)

Baseline

Participant ID _____
Date _____
(MM-DD-YYYY)

Anthropometric Data

Height (cm) _____
Weight (kg) _____
BMI _____

DEXA

Body Fat % _____
Lean Body Mass (kg) _____
Bone Mass (kg) _____

Laboratory

Total Cholesterol _____
LDL _____
HDL _____
AST _____
ALT _____
ALP _____
Calcium _____
Chloride _____
Potassium _____
Sodium _____
BUN _____
Creatinine _____
Insulin _____
Glucose _____
HOMA _____

% beta	_____
% sensitivity	_____
Beta-hydroxybutyrate (mmol/L)	_____
Beta-hydroxybutyrate (mg/dL)	_____

Cognitive Testing

ADAS-Cog	_____
	(0 - 70)
MMSE	_____
	(0 - 30)

MRS

Is MRS scan applicable?	<input type="radio"/> No <input type="radio"/> Yes
N-Acetylaspartate	_____
Glutamate/Glutamine	_____
Lactate	_____
Glutathione	_____
Creatine	_____

Month 1

Participant ID _____
Date _____
(MM-DD-YYYY)

Anthropometric Data

Height (cm) _____
Weight (kg) _____
BMI _____

Laboratory

Insulin _____
Beta-hydroxybutyrate (mmol/L) _____
Beta-hydroxybutyrate (mg/dL) _____

Month 2

Participant ID _____
Date _____
(MM-DD-YYYY)

Anthropometric Data

Height (cm) _____
Weight (kg) _____
BMI _____

Laboratory

Insulin _____
Beta-hydroxybutyrate (mmol/L) _____
Beta_hydroxybutyrate (mg/dL) _____

Post Intervention

Participant ID _____
Date _____
(MM-DD-YYYY)

Anthropometric Data

Height (cm) _____
Weight (kg) _____
BMI _____

DEXA

Body Fat % _____
Lean Body Mass (kg) _____
Bone Mass (kg) _____

Laboratory

Total Cholesterol _____
LDL _____
HDL _____
AST _____
ALT _____
ALP _____
Calcium _____
Chloride _____
Potassium _____
Sodium _____
BUN _____
Creatinine _____
Insulin _____
Glucose _____
HOMA _____

% beta	_____
% sensitivity	_____
Beta-hydroxybutyrate (mmol/L)	_____
Beta-hydroxybutyrate (mg/dL)	_____

Cognitive Testing

ADAS-Cog	_____
	(0 - 70)
MMSE	_____
	(0 - 30)

MRS

Is MRS scan applicable?	<input type="radio"/> No <input type="radio"/> Yes
N-Acetylaspartate	_____
Glutamate/Glutamine	_____
Lactate	_____
Glutathione	_____
Creatine	_____

Washout

Participant ID _____
Date _____
(MM-DD-YYYY)

Anthropometric Data

Height (cm) _____
Weight (kg) _____
BMI _____

Laboratory

Insulin _____
Beta-hydroxybutyrate (mmol/L) _____
Beta-hydroxybutyrate (mg/dL) _____

Cognitive Testing

ADAS-Cog _____
(0 - 70)
MMSE _____
(0 - 30)